(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 1 790 660 A2

(12) **EUROPEAN PATENT APPLICATION**

(43) Date of publication:
30.05.2007 Bulletin 2007/22

(51) Int Cl.:
C07K 14/22 *(2006.01)*

(21) Application number: **06076718.3**

(22) Date of filing: **28.02.2001**

(84) Designated Contracting States:
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR

(30) Priority: **28.02.2000 GB 0004695**
13.11.2000 GB 0027675

(62) Document number(s) of the earlier application(s) in accordance with Art. 76 EPC:
01914109.2 / 1 259 627

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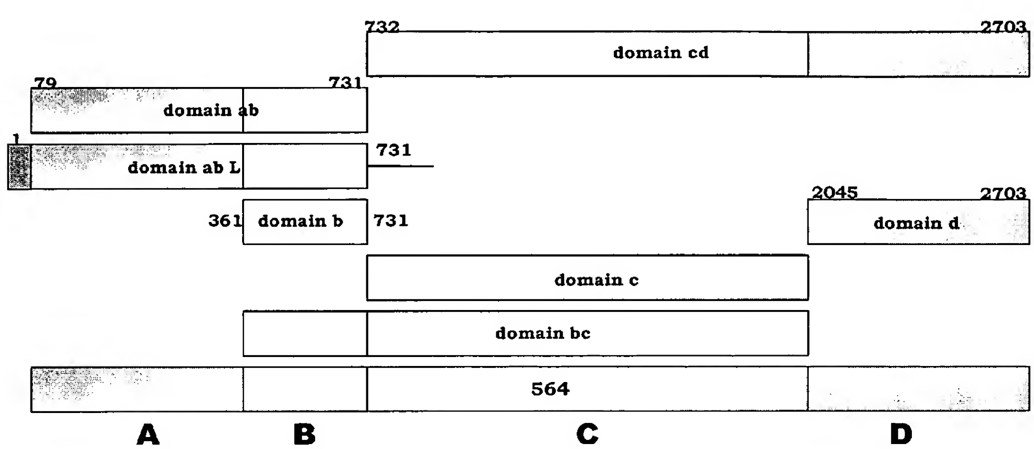
Remarks:
- This application was filed on 13 - 09 - 2006 as a divisional application to the application mentioned under INID code 62.
- The sequence listing, which is published as annex to the application documents, was filed after the date of filing. The applicant has declared that it does not include matter which goes beyond the content of the application as filed.

(54) Heterologous expression of neisserial proteins

(57) Alternative approaches to the heterologous expression of the proteins of *Neisseria meningitidis* and *Neisseria gonorrhoeae*. These approaches typically affect the level of expression, the ease of purification, the cellular localisation, and/or the immunological properties of the expressed protein.

FIGURE 8



Printed by Jouve, 75001 PARIS (FR)

Description

TECHNICAL FIELD

[0001] This invention is in the field of protein expression. In particular, it relates to the heterologous expression of proteins from *Neisseria* (*e.g. N.gonorrhoeae* or, preferably, *N.meningitidis*).

BACKGROUND ART

[0002] International patent applications WO99/24578, WO99/36544, WO99/57280 and WO00/22430 disclose proteins from *Neisseria meningitidis* and *Neisseria gonorrhoeae.* These proteins are typically described as being expressed in *E.coli (i. e.* heterologous expression) as either N-terminal GST-fusions or C-terminal His-tag fusions, although other expression systems, including expression in native *Neisseria,* are also disclosed.

[0003] It is an object of the present invention to provide alternative and improved approaches for the heterologous expression of these proteins. These approaches will typically affect the level of expression, the ease of purification, the cellular localisation of expression, and/or the immunological properties of the expressed protein.

DISCLOSURE OF THE INVENTION

Nomenclature herein

[0004] The 2166 protein sequences disclosed in WO99/24578, WO99/36544 and WO99/57280 are referred to herein by the following SEQ# numbers:

Application	Protein sequences	SEQ# herein
WO99/24578	Even SEQ IDs 2-892	SEQ#s 1-446
WO99/36544	Even SEQ IDs 2-90	SEQ#s 447-491
WO99/57280	Even SEQ IDs 2-3020 Even SEQ IDs 3040-3114 SEQ IDs 3115-3241	SEQ#s 492-2001 SEQ#s 2002-2039 SEQ#s 2040-2166

[0005] In addition to this SEQ# numbering, the naming conventions used in WO99/24578, WO99/36544 and WO99/57280 are also used (*e.g.* 'ORF4', 'ORF40', 'ORF40-1' *etc.* as used in WO99/24578 and WO99/36544; 'm919', 'g919' and 'a919' *etc.* as used in WO99/57280).

[0006] The 2160 proteins NMB0001 to NMB2160 from Tettelin et al. [Science (2000) 287:1809-1815] are referred to herein as SEQ#s 2167-4326 [see also WO00/66791].

[0007] The term 'protein of the invention' as used herein refers to a protein comprising:

(a) one of sequences SEQ#s 1-4326; or
(b) a sequence having sequence identity to one of SEQ#s 1-4326; or
(c) a fragment of one of SEQ#s 1-4326.

[0008] The degree of 'sequence identity' referred to in (b) is preferably greater than 50% *(eg.* 60%, 70%, 80%, 90%, 95%, 99% or more). This includes mutants and allelic variants [e.g. see WO00/66741]. Identity is preferably determined by the Smith-Waterman homology search algorithm as implemented in the MPSRCH program (Oxford Molecular), using an affine gap search with parameters *gap open penalty=12* and *gap extension penalty=1.* Typically, 50% identity or more between two proteins is considered to be an indication of functional equivalence.

[0009] The 'fragment' referred to in (c) should comprise at least n consecutive amino acids from one of SEQ#s 1-4326 and, depending on the particular sequence, n is 7 or more *(eg.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). Preferably the fragment comprises an epitope from one of SEQ#s 1-4326. Preferred fragments are those disclosed in WO00/71574 and WO01/04316.

[0010] Preferred proteins of the invention are found in *N.meningitidis* serogroup B.

[0011] Preferred proteins for use according to the invention are those of serogroup B *N.meningitidis* strain 2996 or strain 394/98 (a New Zealand strain). Unless otherwise stated, proteins mentioned herein are from *N.meningitidis* strain 2996. It will be appreciated, however, that the invention is not in general limited by strain. References to a particular

protein (e.g. '287', '919' *etc.*) may be taken to include that protein from any strain.

Non-fusion expression

[0012] In a first approach to heterologous expression, no fusion partner is used, and the native leader peptide (if present) is used. This will typically prevent any 'interference' from fusion partners and may alter cellular localisation and/or post-translational modification and/or folding in the heterologous host.

[0013] Thus the invention provides a method for the heterologous expression of a protein of the invention, in which (a) no fusion partner is used, and (b) the protein's native leader peptide (if present) is used.

[0014] The method will typically involve the step of preparing an vector for expressing a protein of the invention, such that the first expressed amino acid is the first amino acid (methionine) of said protein, and last expressed amino acid is the last amino acid of said protein (*i.e.* the codon preceding the native STOP codon).

[0015] This approach is preferably used for the expression of the following proteins using the native leader peptide: 111, 149, 206, 225-1, 235, 247-1, 274, 283, 286, 292, 401, 406, 502-1, 503, 519-1, 525-1, 552, 556, 557, 570, 576-1, 580, 583, 664, 759, 907, 913, 920-1, 936-1, 953, 961, 983, 989, Orf4, Orf7-1, Orf9-1, Orf23, Orf25, Orf37, Orf38, Orf40, Orf40.1, Orf40.2, Orf72-1, Orf76-1, Orf85-2, Orf91, Orf97-1, Orf119, Orf143.1, NMB0109 and NMB2050. The suffix 'L' used herein in the name of a protein indicates expression in this manner using the native leader peptide.

[0016] Proteins which are preferably expressed using this approach using no fusion partner and which have no native leader peptide include: 008, 105, 117-1, 121-1, 122-1, 128-1, 148, 216, 243, 308, 593, 652, 726, 926, 982, Orf83-1 and Orf143-1.

[0017] Advantageously, it is used for the expression of ORF25 or ORF40, resulting in a protein which induces better anti-bactericidal antibodies than GST- or His-fusions.

[0018] This approach is particularly suited for expressing lipoproteins.

Leader-peptide substitution

[0019] In a second approach to heterologous expression, the native leader peptide of a protein of the invention is replaced by that of a different protein. In addition, it is preferred that no fusion partner is used. Whilst using a protein's own leader peptide in heterologous hosts can often localise the protein to its 'natural' cellular location, in some cases the leader sequence is not efficiently recognised by the heterologous host. In such cases, a leader peptide known to drive protein targeting efficiently can be used instead.

[0020] Thus the invention provides a method for the heterologous expression of a protein of the invention, in which (a) the protein's leader peptide is replaced by the leader peptide from a different protein and, optionally, (b) no fusion partner is used.

[0021] The method will typically involve the steps of: obtaining nucleic acid encoding a protein of the invention; manipulating said nucleic acid to remove nucleotides that encode the protein's leader peptide and to introduce nucleotides that encode a different protein's leader peptide. The resulting nucleic acid may be inserted into an expression vector, or may already be part of an expression vector. The expressed protein will consist of the replacement leader peptide at the N-terminus, followed by the protein of the invention minus its leader peptide.

[0022] The leader peptide is preferably from another protein of the invention (e.g. one of SEQ#s 1-4326), but may also be from an *E.coli* protein (*e.g.* the OmpA leader peptide) or an *Erwinia carotovora* protein (*e.g.* the PelB leader peptide), for instance.

[0023] A particularly useful replacement leader peptide is that of ORF4. This leader is able to direct lipidation in *E.coli,* improving cellular localisation, and is particularly useful for the expression of proteins 287, 919 and ΔG287. The leader peptide and N-terminal domains of 961 are also particularly useful.

[0024] Another useful replacement leader peptide is that of *E.coli* OmpA. This leader is able to direct membrane localisation of *E.coli.* It is particularly advantageous for the expression of ORF1, resulting in a protein which induces better anti-bactericidal antibodies than both fusions and protein expressed from its own leader peptide.

[0025] Another useful replacement leader peptide is MKKYLFSAA. This can direct secretion into culture medium, and is extremely short and active. The use of this leader peptide is not restricted to the expression of Neisserial proteins - it may be used to direct the expression of any protein (particularly bacterial proteins).

Leader-peptide deletion

[0026] In a third approach to heterologous expression, the native leader peptide of a protein of the invention is deleted. In addition, it is preferred that no fusion partner is used.

[0027] Thus the invention provides a method for the heterologous expression of a protein of the invention, in which (a) the protein's leader peptide is deleted and, optionally, (b) no fusion partner is used.

[0028] The method will typically involve the steps of: obtaining nucleic acid encoding a protein of the invention; manipulating said nucleic acid to remove nucleotides that encode the protein's leader peptide. The resulting nucleic acid may be inserted into an expression vector, or may already be part of an expression vector. The first amino acid of the expressed protein will be that of the mature native protein.
[0029] This method can increase the levels of expression. For protein 919, for example, expression levels in *E.coli* are much higher when the leader peptide is deleted. Increased expression may be due to altered localisation in the absence of the leader peptide.
[0030] The method is preferably used for the expression of 919, ORF46, 961, 050-1, 760 and 287.

Domain-based expression

[0031] In a fourth approach to heterologous expression, the protein is expressed as domains. This may be used in association with fusion systems (e.g. GST or His-tag fusions).
[0032] Thus the invention provides a method for the heterologous expression of a protein of the invention, in which (a) at least one domain in the protein is deleted and, optionally, (b) no fusion partner is used.
[0033] The method will typically involve the steps of: obtaining nucleic acid encoding a protein of the invention; manipulating said nucleic acid to remove at least one domain from within the protein. The resulting nucleic acid may be inserted into an expression vector, or may already be part of an expression vector. Where no fusion partners are used, the first amino acid of the expressed protein will be that of a domain of the protein.
[0034] A protein is typically divided into notional domains by aligning it with known sequences in databases and then determining regions of the protein which show different alignment patterns from each other.
[0035] The method is preferably used for the expression of protein 287. This protein can be notionally split into three domains, referred to as A B & C (see Figure 5). Domain B aligns strongly with IgA proteases, domain C aligns strongly with transferrin-binding proteins, and domain A shows no strong alignment with database sequences. An alignment of polymorphic forms of 287 is disclosed in WO00/66741.
[0036] Once a protein has been divided into domains, these can be (a) expressed singly (b) deleted from with the protein e.g. protein ABCD $\rightarrow$ ABD, ACD, BCD *etc.* or (c) rearranged e.g. protein ABC $\rightarrow$ ACB, CAB *etc.* These three strategies can be combined with fusion partners is desired.
[0037] ORF46 has also been notionally split into two domains - a first domain (amino acids 1-433) which is well-conserved between species and serogroups, and a second domain (amino acids 433-608) which is not well-conserved. The second domain is preferably deleted. An alignment of polymorphic forms of ORF46 is disclosed in WO00/66741.
[0038] Protein 564 has also been split into domains (Figure 8), as have protein 961 (Figure 12) and protein 502 (amino acids 28-167 of the MC58 protein).

Hybrid proteins

[0039] In a fifth approach to heterologous expression, two or more (e.g. 3, 4, 5, 6 or more) proteins of the invention are expressed as a single hybrid protein. It is preferred that no non-Neisserial fusion partner (e.g. GST or poly-His) is used.
[0040] This offers two advantages. Firstly, a protein that may be unstable or poorly expressed on its own can be assisted by adding a suitable hybrid partner that overcomes the problem. Secondly, commercial manufacture is simplified - only one expression and purification need be employed in order to produce two separately-useful proteins.
[0041] Thus the invention provides a method for the simultaneous heterologous expression of two or more proteins of the invention, in which said two or more proteins of the invention are fused (i.e. they are translated as a single polypeptide chain).
[0042] The method will typically involve the steps of: obtaining a first nucleic acid encoding a first protein of the invention; obtaining a second nucleic acid encoding a second protein of the invention; ligating the first and second nucleic acids. The resulting nucleic acid may be inserted into an expression vector, or may already be part of an expression vector.
[0043] Preferably, the constituent proteins in a hybrid protein according to the invention will be from the same strain.
[0044] The fused proteins in the hybrid may be joined directly, or may be joined via a linker peptide *e.g.* via a poly-glycine linker (*i.e.* G_n where n = 3, 4, 5, 6, 7, 8, 9, 10 or more) or via a short peptide sequence which facilitates cloning. It is evidently preferred not to join a ΔG protein to the C-terminus of a poly-glycine linker.
[0045] The fused proteins may lack native leader peptides or may include the leader peptide sequence of the N-terminal fusion partner.
[0046] The method is well suited to the expression of proteins orf1, orf4, orf25, orf40, Orf46/46.1, orf83, 233, 287, 292L, 564, 687, 741, 907, 919, 953, 961 and 983.
[0047] The 42 hybrids indicated by 'X' in the following table of form NH_2-A-B-COOH are preferred:

↓A B→	ORF46.1	287	741	919	953	961	983
ORF46.1		X	X	X	X	X	X
287	X		X	X	X	X	X
741	X	X		X	X	X	X
919	X	X	X		X	X	X
953	X	X	X	X		X	X
961	X	X	X	X	X		X
983	X	X	X	X	X	X	

[0048] Preferred proteins to be expressed as hybrids are thus ORF46.1, 287, 741, 919, 953, 961 and 983. These may be used in their essentially full-length form, or poly-glycine deletions (ΔG) forms may be used (*e.g.* ΔG-287, ΔGTbp2, ΔG741, ΔG983 *etc.*), or truncated forms may be used (*e.g.* Δ1-287, Δ2-287 *etc.*), or domain-deleted versions may be used (*e.g.* 287B, 287C, 287BC, $ORF46_{1\text{-}433}$, $ORF46_{433\text{-}608}$, ORF46, 961c *etc.*).

[0049] Particularly preferred are: (a) a hybrid protein comprising 919 and 287; (b) a hybrid protein comprising 953 and 287; (c) a hybrid protein comprising 287 and ORF46.1; (d) a hybrid protein comprising ORF1 and ORF46.1; (e) a hybrid protein comprising 919 and ORF46.1; (f) a hybrid protein comprising ORF46.1 and 919; (g) a hybrid protein comprising ORF46.1, 287 and 919; (h) a hybrid protein comprising 919 and 519; and (i) a hybrid protein comprising ORF97 and 225. Further embodiments are shown in Figure 14.

[0050] Where 287 is used, it is preferably at the C-terminal end of a hybrid; if it is to be used at the N-terminus, if is preferred to use a ΔG form of 287 is used (e.g. as the N-terminus of a hybrid with ORF46.1, 919, 953 or 961).

[0051] Where 287 is used, this is preferably from strain 2996 or from strain 394/98.

[0052] Where 961 is used, this is preferably at the N-terminus. Domain forms of 961 may be used.

[0053] Alignments of polymorphic forms of ORF46, 287, 919 and 953 are disclosed in WO00/66741. Any of these polymorphs can be used according to the present invention.

Temperature

[0054] In a sixth approach to heterologous expression, proteins of the invention are expressed at a low temperature.

[0055] Expressed Neisserial proteins (e.g. 919) may be toxic to *E.coli,* which can be avoided by expressing the toxic protein at a temperature at which its toxic activity is not manifested.

[0056] Thus the present invention provides a method for the heterologous expression of a protein of the invention, in which expression of a protein of the invention is carried out at a temperature at which a toxic activity of the protein is not manifested.

[0057] A preferred temperature is around 30°C. This is particularly suited to the expression of 919.

Mutations

[0058] As discussed above, expressed Neisserial proteins may be toxic to *E coli.* This toxicity can be avoided by mutating the protein to reduce or eliminate the toxic activity. In particular, mutations to reduce or eliminate toxic enzymatic activity can be used, preferably using site-directed mutagenesis.

[0059] In a seventh approach to heterologous expression, therefore, an expressed protein is mutated to reduce or eliminate toxic activity.

[0060] Thus the invention provides a method for the heterologous expression of a protein of the invention, in which protein is mutated to reduce or eliminate toxic activity.

[0061] The method is preferably used for the expression of protein 907, 919 or 922. A preferred mutation in 907 is at Glu-117 (e.g. Glu→Gly); preferred mutations in 919 are at Glu-255 (e.g. Glu→Gly) and/or Glu-323 (e.g. Glu→Gly); preferred mutations in 922 are at Glu-164 *(e.g.* Glu→Gly), Ser-213 (e.g. Ser→Gly) and/or Asn-348 (e.g. Asn→Gly).

Alternative vectors

[0062] In a eighth approach to heterologous expression, an alternative vector used to express the protein. This may be to improve expression yields, for instance, or to utilise plasmids that are already approved for GMP use.

[0063] Thus the invention provides a method for the heterologous expression of a protein of the invention, in which

an alternative vector is used. The alternative vector is preferably pSM214, with no fusion partners. Leader peptides may or may not be included.

[0064] This approach is particularly useful for protein 953. Expression and localisation of 953 with its native leader peptide expressed from pSM214 is much better than from the pET vector.

[0065] pSM214 may also be used with: ΔG287, Δ2-287, Δ3-287, Δ4-287, Orf46.1, 961L, 961, 96 1 (MC58), 96 1 c, 96 1 c-L, 919, 953 and ΔG287-Orf46.1.

[0066] Another suitable vector is pET-24b (Novagen; uses kanamycin resistance), again using no fusion partners. pET-24b is preferred for use with: ΔG287K, Δ2-287K, Δ3-287K, Δ4-287K,

[0067] Orf46.1-K, Orf46A-K, 961-K (MC58), 961a-K, 961b-K, 961c-K, 961c-L-K, 961d-K, ΔG287-919-K, ΔG287-Orf46.1-K and ΔG287-961-K.

Multimeric form

[0068] In a ninth approach to heterologous expression, a protein is expressed or purified such that it adopts a particular multimeric form.

[0069] This approach is particularly suited to protein 953. Purification of one particular multimeric form of 953 (the monomeric form) gives a protein with greater bactericidal activity than other forms (the dimeric form).

[0070] Proteins 287 and 919 may be purified in dimeric forms.

[0071] Protein 961 may be purified in a 180kDa oligomeric form (e.g. a tetramer).

Lipidation

[0072] In a tenth approach to heterologous expression, a protein is expressed as a lipidated protein.

[0073] Thus the invention provides a method for the heterologous expression of a protein of the invention, in which the protein is expressed as a lipidated protein.

[0074] This is particularly useful for the expression of 919, 287, ORF4, 406, 576-1, and ORF25. Polymorphic forms of 919, 287 and ORF4 are disclosed in WO00/66741.

[0075] The method will typically involve the use of an appropriate leader peptide without using an N-terminal fusion partner.

C-terminal deletions

[0076] In an eleventh approach to heterologous expression, the C-terminus of a protein of the invention is mutated. In addition, it is preferred that no fusion partner is used.

[0077] Thus the invention provides a method for the heterologous expression of a protein of the invention, in which (a) the protein's C-terminus region is mutated and, optionally, (b) no fusion partner is used.

[0078] The method will typically involve the steps of: obtaining nucleic acid encoding a protein of the invention; manipulating said nucleic acid to mutate nucleotides that encode the protein's C-terminus portion. The resulting nucleic acid may be inserted into an expression vector, or may already be part of an expression vector. The first amino acid of the expressed protein will be that of the mature native protein.

[0079] The mutation may be a substitution, insertion or, preferably, a deletion.

[0080] This method can increase the levels of expression, particularly for proteins 730, ORF29 and ORF46. For protein 730, a C-terminus region of around 65 to around 214 amino acids may be deleted; for ORF46, the C-terminus region of around 175 amino acids may be deleted; for ORF29, the C-terminus may be deleted to leave around 230-370 N-terminal amino acids.

Leader peptide mutation

[0081] In a twelfth approach to heterologous expression, the leader peptide of the protein is mutated. This is particularly useful for the expression of protein 919.

[0082] Thus the invention provides a method for the heterologous expression of a protein of the invention, in which the protein's leader peptide is mutated.

[0083] The method will typically involve the steps of: obtaining nucleic acid encoding a protein of the invention; and manipulating said nucleic acid to mutate nucleotides within the leader peptide. The resulting nucleic acid may be inserted into an expression vector, or may already be part of an expression vector.

Poly-glycine deletion

[0084] In a thirteenth approach to heterologous expression, poly-glycine stretches in wild-type sequences are mutated. This enhances protein expression.

[0085] The poly-glycine stretch has the sequence $(Gly)_n$, where n≥4 (e.g. 5, 6, 7, 8, 9 or more). This stretch is mutated to disrupt or remove the $(Gly)_n$. This may be by deletion (*e.g.* CGGGGS→ CGGGS, CGGS, CGS or CS), by substitution (*e.g.* CGGGGS→ CGXGGS, CGXXGS, CGXGXS *etc.*), and/or by insertion (e.g. CGGGGS→ CGGXGGS, CGXGGGS, *etc.*).

[0086] This approach is not restricted to Neisserial proteins - it may be used for any protein (particularly bacterial proteins) to enhance heterologous expression. For Neisserial proteins, however, it is particularly suitable for expressing 287, 741, 983 and Tbp2. An alignment of polymorphic forms of 287 is disclosed in WO00/66741.

[0087] Thus the invention provides a method for the heterologous expression of a protein of the invention, in which (a) a poly-glycine stretch within the protein is mutated.

[0088] The method will typically involve the steps of: obtaining nucleic acid encoding a protein of the invention; and manipulating said nucleic acid to mutate nucleotides that encode a poly-glycine stretch within the protein sequence. The resulting nucleic acid may be inserted into an expression vector, or may already be part of an expression vector.

[0089] Conversely, the opposite approach (i.e. introduction of poly-glycine stretches) can be used to suppress or diminish expression of a given heterologous protein.

Heterologous host

[0090] Whilst expression of the proteins of the invention may take place in the native host (i.e. the organism in which the protein is expressed in nature), the present invention utilises a heterologous host. The heterologous host may be prokaryotic or eukaryotic. It is preferably *E.coli,* but other suitable hosts include *Bacillus subtilis, Vibrio cholerae, Salmonella typhi, Salmonenna typhimurium, Neisseria meningitidis, Neisseria gonorrhoeae, Neisseria lactamica, Neisseria cinerea, Mycobateria* (*e.g. M.tuberculosis*), yeast *etc.*

***Vectors* etc.**

[0091] As well as the methods described above, the invention provides (a) nucleic acid and vectors useful in these methods (b) host cells containing said vectors (c) proteins expressed or expressable by the methods (d) compositions comprising these proteins, which may be suitable as vaccines, for instance, or as diagnostic reagents, or as immunogenic compositions (e) these compositions for use as medicaments (e.g. as vaccines) or as diagnostic reagents (f) the use of these compositions in the manufacture of (1) a medicament for treating or preventing infection due to Neisserial bacteria (2) a diagnostic reagent for detecting the presence of Neisserial bacteria or of antibodies raised against Neisserial bacteria, and/or (3) a reagent which can raise antibodies against Neisserial bacteria and (g) a method of treating a patient, comprising administering to the patient a therapeutically effective amount of these compositions.

Sequences

[0092] The invention also provides a protein or a nucleic acid having any of the sequences set out in the following examples. It also provides proteins and nucleic acid having sequence identity to these. As described above, the degree of 'sequence identity' is preferably greater than 50% (eg. 60%, 70%, 80%, 90%, 95%, 99% or more).

[0093] Furthermore, the invention provides nucleic acid which can hybridise to the nucleic acid disclosed in the examples, preferably under "high stringency" conditions (*eg.* 65°C in a 0.1xSSC, 0.5% SDS solution).

[0094] The invention also provides nucleic acid encoding proteins according to the invention.

[0095] It should also be appreciated that the invention provides nucleic acid comprising sequences complementary to those described above (*eg.* for antisense or probing purposes).

[0096] Nucleic acid according to the invention can, of course, be prepared in many ways *(eg.* by chemical synthesis, from genomic or cDNA libraries, from the organism itself *etc.)* and can take various forms *(eg.* single stranded, double stranded, vectors, probes *etc.).*

[0097] In addition, the term "nucleic acid" includes DNA and RNA, and also their analogues, such as those containing modified backbones, and also peptide nucleic acids (PNA) *etc.*

BRIEF DESCRIPTION OF DRAWINGS

[0098]

Figures 1 and 2 show constructs used to express proteins using heterologous leader peptides.

Figure 3 shows expression data for ORF1, and Figure 4 shows similar data for protein 961.

Figure 5 shows domains of protein 287, and Figures 6 & 7 show deletions within domain A.

Figure 8 shows domains of protein 564.

Figure 9 shows the *PhoC* reporter gene driven by the 919 leader peptide, and Figure 10 shows the results obtained using mutants of the leader peptide.

Figure 11 shows insertion mutants of protein 730 (A: 730-C1; B: 730-C2).

Figure 12 shows domains of protein 961.

Figure 13 shows SDS-PAGE of ΔG proteins. Dots show the main recombinant product.

Figure 14 shows 26 hybrid proteins according to the invention.

MODES FOR CARRYING OUT THE INVENTION

Example 1- 919 and its leader peptide

[0099] Protein 919 from *N.meningitidis* (serogroup B, strain 2996) has the following sequence:

```
  1 MKKYLFRAAL YGIAAAILAA CQSKSIQTFP QPDTSVINGP DRPVGIPDPA
 51 GTTVGGGGAV YTVVPHLSLP HWAAQDFAKS LQSFRLGCAN LKNRQGWQDV
101 CAQAFQTPVH SFQAKQFFER YFTPWQVAGN GSLAGTVTGY YEPVLKGDDR
151 RTAQARFPIY GIPDDFISVP LPAGLRSGKA LVRIRQTGKN SGTIDNTGGT
201 HTADLSRFPI TARTTAIKGR FEGSRFLPYH TRNQINGGAL DGKAPILGYA
251 EDPVELFFMH IQGSGRLKTP SGKYIRIGYA DKNEHPYVSI GRYMADKGYL
301 KLGQTSMQGI KAYMRQNPQR LAEVLGQNPS YIFFRELAGS SNDGPVGALG
351 TPLMGEYAGA VDRHYITLGA PLFVATAHPV TRKALNRLIM AQDTGSAIKG
401 AVRVDYFWGY GDEAGELAGK QKTTGYVWQL LPNGMKPEYR P*
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[0100] The leader peptide is underlined.

[0101] The sequences of 919 from other strains can be found in Figures 7 and 18 of WO00/66741.

[0102] Example 2 of WO99/57280 discloses the expression of protein 919 as a His-fusion in *E.coli.*

[0103] The protein is a good surface-exposed immunogen.

[0104] Three alternative expression strategies were used for 919:

1) 919 without its leader peptide (and without the mature N-terminal cysteine) and without any fusion partner ('919$^{\text{untagged}}$'):

```
  1  QSKSIQTFP QPDTSVINGP DRPVGIPDPA GTTVGGGGAV YTVVPHLSLP
 50 HWAAQDFAKS LQSFRLGCAN LKNRQGWQDV CAQAFQTPVH SFQAKQFFER
100 YFTPWQVAGN GSLAGTVTGY YEPVLKGDDR RTAQARFPIY GIPDDFISVP
150 LPAGLRSGKA LVRIRQTGKN SGTIDNTGGT HTADLSRFPI TARTTAIKGR
200 FEGSRFLPYH TRNQINGGAL DGKAPILGYA EDPVELFFMH IQGSGRLKTP
250 SGKYIRIGYA DKNEHPYVSI GRYMADKGYL KLGQTSMQGI KAYMRQNPQR
300 LAEVLGQNPS YIFFRELAGS SNDGPVGALG TPLMGEYAGA VDRHYITLGA
350 PLFVATAHPV TRKALNRLIM AQDTGSAIKG AVRVDYFWGY GDEAGELAGK
400 QKTTGYVWQL LPNGMKPEYR P*
```

The leader peptide and cysteine were omitted by designing the 5'-end amplification primer downstream from the predicted leader sequence.

2) 919 with its own leader peptide but without any fusion partner ('919L'); and

3) 919 with the leader peptide (MKTFFKTLSAAALALILAA) from ORF4 ('919LOrf4').

```
  1   MKTFFKTLS AAALALILAA CQSKSIQTFP QPDTSVINGP DRPVGIPDPA
 50  GTTVGGGGAV YTVVPHLSLP HWAAQDFAKS LQSFRLGCAN LKNRQGWQDV
100  CAQAFQTPVH SFQAKQFFER YFTPWQVAGN GSLAGTVTGY YEPVLKGDDR
150  RTAQARFPIY GIPDDFISVP LPAGLRSGKA LVRIRQTGKN SGTIDNTGGT
200  HTADLSRFPI TARTTAIKGR FEGSRFLPYH TRNQINGGAL DGKAPILGYA
250  EDPVELFFMH IQGSGRLKTP SGKYIRIGYA DKNEHPYVSI GRYMADKGYL
300  KLGQTSMQGI KSYMRQNPQR LAEVLGQNPS YIFFRELAGS SNDGPVGALG

350  TPLMGEYAGA VDRHYITLGA PLFVATAHPV TRKALNRLIM AQDTGSAIKG
400  AVRVDYFWGY GDEAGELAGK QKTTGYVWQL LPNGMKPEYR P*
```

To make this construct, the entire sequence encoding the ORF4 leader peptide was included in the 5'-primer as a tail (primer 919Lorf4 For). A *Nhe*I restriction site was generated by a double nucleotide change in the sequence coding for the ORF4 leader (no amino acid changes), to allow different genes to be fused to the ORF4 leader peptide sequence. A stop codon was included in all the 3'-end primer sequences.

[0105] All three forms of the protein were expressed and could be purified.

[0106] The '919L' and '919LOrf4' expression products were both lipidated, as shown by the incorporation of [^{3}H]-palmitate label. 919^{untagged} did not incorporate the ^{3}H label and was located intracellularly.

[0107] 919LOrf4 could be purified more easily than 919L. It was purified and used to immunise mice. The resulting sera gave excellent results in FACS and ELISA tests, and also in the bactericidal assay. The lipoprotein was shown to be localised in the outer membrane.

[0108] 919^{untagged} gave excellent ELISA titres and high serum bactericidal activity. FACS confirmed its cell surface location.

Example 2 — 919 and expression temperature

[0109] Growth of *E.coli* expressing the 919LOrf4 protein at 37°C resulted in lysis of the bacteria. In order to overcome this problem, the recombinant bacteria were grown at 30°C. Lysis was prevented without preventing expression.

Example 3 - mutation of 907, 919 and 922

[0110] It was hypothesised that proteins 907, 919 and 922 are murein hydrolases, and more particularly lytic transglycosylases. Murein hydrolases are located on the outer membrane and participate in the degradation of peptidoglycan.

[0111] The purified proteins 919^{untagged}, 919Lorf4, 919-His (*i.e.* with a C-terminus His-tag) and 922-His were thus tested for murein hydrolase activity [Ursinus & Holtje (1994) J.Bact. 176:338-343]. Two different assays were used, one determining the degradation of insoluble murein sacculus into soluble muropeptides and the other measuring breakdown of poly(MurNAc-GlcNAc)$_{n>30}$ glycan strands.

[0112] The first assay uses murein sacculi radiolabelled with meso-2,6-diamino-3,4,5-[^{3}H]pimelic acid as substrate. Enzyme (3-10 μg total) was incubated for 45 minutes at 37°C in a total volume of 100μl comprising 10mM Tris-maleate (pH 5.5), 10mM $MgCl_2$, 0.2% v/v Triton X-100 and [^{3}H]A_2pm labelled murein sacculi (about 10000cpm). The assay mixture was placed on ice for 15 minutes with 100 μl of 1% w/v N-acetyl-N,N,N-trimethylammonium for 15 minutes and precipitated material pelleted by centrifugation at 10000g for 15 minutes. The radioactivity in the supernatant was measured by liquid scintillation counting. *E.coli* soluble lytic transglycosylase Slt70 was used as a positive control for the assay; the negative control comprised the above assay solution without enzyme.

[0113] All proteins except 919-His gave positive results in the first assay.

[0114] The second assay monitors the hydrolysis of poly(MurNAc-GlcNAc)glycan strands. Purified strands, poly(MurNAc-GlcNAc)$_{n>30}$ labelled with N-acetyl-D-1-[^{3}H]glucosamine were incubated with 3μg of 919L in 10 mM Tris-maleate (pH 5.5), 10 mM $MgCl_2$ and 0.2% v/v Triton X-100 for 30 min at 37°C. The reaction was stopped by boiling for 5 minutes and the pH of the sample adjusted to about 3.5 by addition of 10μl of 20% v/v phosphoric acid. Substrate and product were separated by reversed phase HPLC on a Nucleosil 300 C_{18} column as described by Harz et. al. [Anal. Biochem. (1990) 190:120-128]. The *E.coli* lytic transglycosylase Mlt A was used as a positive control in the assay. The negative control was performed in the absence of enzyme.

[0115] By this assay, the ability of 919LOrf4 to hydrolyse isolated glycan strands was demonstrated when anhydro-disaccharide subunits were separated from the oligosaccharide by HPLC.

[0116] Protein 919Lorf4 was chosen for kinetic analyses. The activity of 919Lorf4 was enhanced 3.7-fold by the addition of 0.2% v/v Triton X-100 in the assay buffer. The presence of Triton X-100 had no effect on the activity of $919^{untagged}$. The effect of pH on enzyme activity was determined in Tris-Maleate buffer over a range of 5.0 to 8.0. The optimal pH for the reaction was determined to be 5.5. Over the temperature range 18°C to 42°C, maximum activity was observed at 37°C. The effect of various ions on murein hydrolase activity was determined by performing the reaction in the presence of a variety of ions at a final concentration of 10mM. Maximum activity was found with Mg^{2+}, which stimulated activity 2.1-fold. Mn^{2+} and Ca^{2+} also stimulated enzyme activity to a similar extent while the addition Ni^{2+} and EDTA had no significant effect. In contrast, both $Fe^{2+}$and Zn^{2+} significantly inhibited enzyme activity.

[0117] The structures of the reaction products resulting from the digestion of unlabelled *E.coli* murein sacculus were analysed by reversed-phase HPLC as described by Glauner [Anal. Biochem. (1988) 172:451-464]. Murein sacculi digested with the muramidase Cellosyl were used to calibrate and standardise the Hypersil ODS column. The major reaction products were 1,6 anhydrodisaccharide tetra and tri peptides, demonstrating the formation of 1,6 anhydromuraminic acid intramolecular bond.

[0118] These results demonstrate experimentally that 919 is a murein hydrolase and in particular a member of the lytic transglycosylase family of enzymes. Furthermore the ability of 922-His to hydrolyse murein sacculi suggests this protein is also a lytic transglycosylase.

[0119] This activity may help to explain the toxic effects of 919 when expressed in *E.coli.*

[0120] In order to eliminate the enzymatic activity, rational mutagenesis was used. 907, 919 and 922 show fairly low homology to three membrane-bound lipidated murein lytic transglycosylases from *E.coli*:

919 (441aa) is 27.3% identical over 440aa overlap to *E.coli* MLTA (P46885);
922 (369aa) is 38.7% identical over 310aa overlap to *E.coli* MLTB (P41052); and
907-2 (207aa) is 26.8% identical over 149aa overlap to *E.coli* MLTC (P52066).

907-2 also shares homology with *E.coli* MLTD (P23931) and Slt70 (P03810), a soluble lytic transglycosylase that is located in the periplasmic space. No significant sequence homology can be detected among 919, 922 and 907-2, and the same is true among the corresponding MLTA, MLTB and MLTC proteins.

[0121] Crystal structures are available for Slt70 [1QTEA; 1QTEB; Thunnissen et al. (1995) Biochemistry 34: 12729-12737] and for Slt35 [1LTM; 1QUS; 1QUT; van Asselt et al. (1999) Structure Fold Des 7:1167-80] which is a soluble form of the 40kDa MLTB.

[0122] The catalytic residue (a glutamic acid) has been identified for both Slt70 and MLTB.

[0123] In the case of Slt70, mutagenesis studies have demonstrated that even a conservative substitution of the catalytic Glu505 with a glutamine (Gln) causes the complete loss of enzymatic activity. Although Slt35 has no obvious sequence similarity to Slt70, their catalytic domains shows a surprising similarity. The corresponding catalytic residue in MLTB is Glu162.

[0124] Another residue which is believed to play an important role in the correct folding of the enzymatic cleft is a well-conserved glycine (Gly) downstream of the glutamic acid. Recently, Terrak et al. [Mol.Microbiol. (1999) 34:350-64] have suggested the presence of another important residue which is an aromatic amino acid located around 70-75 residues downstream of the catalytic glutamic acid.

[0125] Sequence alignment of Slt70 with 907-2 and of MLTB with 922 were performed in order to identify the corresponding catalytic residues in the MenB antigens.

[0126] The two alignments in the region of the catalytic domain are reported below:

907-2/Slt70:

```
                 90       100         110      ▼120       130       140
907-2.pep       ERRRLLVNIQYESSRAG--LDTQIVLGLIEVESAFRQYAISGVGARGLMQVMPFWKNYIG
                ||  |  |  ::   :|  :  : :::: : |||:   : | ||| ||||:||   ::
slty_ecoli      ERFPLAYNDLFKRYTSGKEIPQSYAMAIARQESAWNPKVKSPVGASGLMQIMPGTATHTV
                    480       490       500    ▲  510       520       530
                                               GLU505
```

922/MLTB

```
                 150       160  ▼  170       180       190       200
922.pep       VAQKYGVPAELIVAVIGIETNYGKNTGSFRVADALATLGFDYPRRAGFFQKELVELLKLA
              : | |||| |:||::||:|| :|:  |: |: ||||||:|:||||| :|: ||  :| :|
mltb_ecoli    AWQVYGVPPEIIVGIIGVETRWGRVMGKTRILDALATLSFNYPRRAEYFSGELETFLLMA
                  150       160 ▲     170       180       190       200
                                GLU162

                 210       220       230       240       250       260
922.pep       KEEGGDVFAFKGSYAGAMGMPQFMPSSYRKWAVDYDGDGHRDIWGNVGDVAASVANYMKQ
              ::|  | : :|||:|||||: ||||||::::|||::|||| ::|  | |: :|||||:|
mltb_ecoli    RDEQDDPLNLKGSFAGAMGYGQFMPSSYKQYAVDFSGDGHINLWDPV-DAIGSVANYFKA
                  210       220       230       240       250       260
```

[0127] From these alignments, it results that the corresponding catalytic glutamate in 907-2 is Glu117, whereas in 922 is Glu164. Both antigens also share downstream glycines that could have a structural role in the folding of the enzymatic cleft (in bold), and 922 has a conserved aromatic residue around 70aa downstream (in bold).

[0128] In the case of protein 919, no 3D structure is available for its *E.coli* homologue MLTA, and nothing is known about a possible catalytic residue. Nevertheless, three amino acids in 919 are predicted as catalytic residues by alignment with MLTA:

919/MLTA

```
              240       250     ▼ 260  □ □  270 □     280       290
919.pep        ALDGKAPILGYAEDPVELFFMHIQGSGRLKTPSGKYIRI-GYADKNEHPYVSIGRYMADK
               ||: |  ||:|::: :: |:| :|||| :    :|: : : :|| || | | |||: : |:
mlta_ecoli.p   ALSDKY-ILAYSNSLMDNFIMDVQGSGYIDFGDGSPLNFFSYAGKNGHAYRSIGKVLIDR
                         170       180       190       200       210

                300       310       320  ▼    330□ □□  340      ◊350    ◊
919.pep        GYLKLGQTSMQGIKSYMRQNPQ-RLAEVLGQNPSYIFFRELAGSSNDGPV-GALGTPLMG
               | :|   : |||:|: : : : : :: |:| ||||::||:   : :     || || ::||:|
mlta_ecoli.p   GEVKKEDMSMQAIRHWGETHSEAEVRELLEQNPSFVFFKPQSFA----PVKGASAVPLVG
             220       230       240       250       260           270

                 360 ▼     o       380            390       400      ◊◊410
919.pep        EYAGAVDRHYITLGAPLFVATAHPVTRKALN-----RLIMAQDTGSAIKGAVRVDYFWGY
               : : | || |  |: |:: :    :    :|     ||::| |:|:|||| : | : |
mlta_ecoli.p   RASVASDRSIIPPGTTLLAEVPLLDNNGKFNGQYELRLMVALDVGGAIKGQ-HFDIYQGI
                   280       290       300       310       320        330

                      420      o
919.pep        GDEAGELAGKQKTTGYVWQLLP
               | |||: ||   :  | || |
mlta_ecoli.p   GPEAGHRAGWYNHYGRVWVLKT
                   340       350
```

[0129] The three possible catalytic residues are shown by the symbol ▼:

1) Glu255 (Asp in MLTA), followed by three conserved glycines (Gly263, Gly265 and Gly272) and three conserved aromatic residues located approximately 75-77 residues downstream. These downstream residues are shown by o.

2) Glu323 (conserved in MLTA), followed by 2 conserved glycines (Gly347 and Gly355) and two conserved aromatic residues located 84-85 residues downstream (Tyr406 or Phe407). These downstream residues are shown by ◇.

3) Asp362 (instead of the expected Glu), followed by one glycine (Gly 369) and a conserved aromatic residue

(Trp428). These downstream residues are shown by O.

[0130] Alignments of polymorphic forms of 919 are disclosed in WO00/66741.

[0131] Based on the prediction of catalytic residues, three mutants of the 919 and one mutant of 907, containing each a single amino acid substitution, have been generated. The glutamic acids in position 255 and 323 and the aspartic acids in position 362 of the 919 protein and the glutamic acid in position 117 of the 907 protein, were replaced with glycine residues using PCR-based SDM. To do this, internal primers containing a codon change from Glu or Asp to Gly were designed:

Primers	Sequences	Codon change
919-E255 for 919-E255 rev	CGAAGACCCCGTCGgtCTTTTTTTATG GTGCATAAAAAAAGacCGACGGGGTCT	GAA → Ggt
919-E323 for 919-E323 rev	AACGCCTCGCCGgtGTTTTGGGTCA TTTGACCCAAAACacCGGCGAGGCG	GAA → Ggt
919-D362 for 919-D362 rev	TGCCGGCGCAGTCGgtCGGCACTACA TAATGTAGTGCCGacCGACTGCGCCG	GAC → Ggt
907-E117 for 907-E117 rev	TGATTGAGGTGGgtAGCGCGTTCCG GGCGGAACGCGCTacCCACCTCAAT	GAA → Ggt
Underlined nucleotides code for glycine; the mutated nucleotides are in lower case.		

[0132] To generate the 919-E255, 919-E323 and 919-E362 mutants, PCR was performed using 20ng of the pET 919-LOrf4 DNA as template, and the following primer pairs:

1) Orf4L for / 919-E255 rev
2) 919-E255 for / 919L rev
3) Orf4L for / 919-E323 rev
4) 919-E323 for / 919L rev
5) Orf4L for / 919-D362 rev
6) 919-D362 for / 919L rev

The second round of PCR was performed using the product of PCR 1-2, 3-4 or 5-6 as template, and as forward and reverse primers the "Orf4L for" and "919L rev" respectively.

For the mutant 907-E117, PCR have been performed using 200ng of chromosomal DNA of the 2996 strain as template and the following primer pairs:

7) 907L for / 907-E117 rev
8) 907-E 117 for / 907L rev

[0133] The second round of PCR was performed using the products of PCR 7 and 8 as templates and the oligos "907L for" and "907L rev" as primers.

[0134] The PCR fragments containing each mutation were processed following the standard procedure, digested with *Nde*I and *Xho*I restriction enzymes and cloned into pET-21b+ vector. The presence of each mutation was confirmed by sequence analysis.

[0135] Mutation of Glu117 to Gly in 907 is carried out similarly, as is mutation of residues Glu164, Ser213 and Asn348 in 922.

[0136] The E255G mutant of 919 shows a 50% reduction in activity; the E323G mutant shows a 70% reduction in activity; the E362G mutant shows no reduction in activity.

Example 4 - multimeric form

[0137] 287-GST, 919^{untagged} and 953-His were subjected to gel filtration for analysis of quaternary structure or preparative purposes. The molecular weight of the native proteins was estimated using either FPLC Superose 12 (H/R 10/30) or Superdex 75 gel filtration columns (Pharmacia). The buffers used for chromatography for 287, 919 and 953 were 50 mM Tris-HCl (pH 8.0), 20 mM Bicine (pH 8.5) and 50 mM Bicine (pH 8.0), respectively.

[0138] Additionally each buffer contained 150-200 mM NaCl and 10% v/v glycerol. Proteins were dialysed against the appropriate buffer and applied in a volume of 200μl. Gel filtration was performed with a flow rate of 0.5 - 2.0 ml/min and

the eluate monitored at 280nm. Fractions were collected and analysed by SDS-PAGE. Blue dextran 2000 and the molecular weight standards ribonuclease A, chymotrypsin A ovalbumin, albumin (Pharmacia) were used to calibrate the column. The molecular weight of the sample was estimated from a calibration curve of K_{av} *vs.* log M_r of the standards. Before gel filtration, 287-GST was digested with thrombin to cleave the GST moiety.

[0139] The estimated molecular weights for 287, 919 and 953-His were 73 kDa, 47 kDa and 43 kDa respectively. These results suggest 919 is monomeric while both 287 and 953 are principally dimeric in their nature. In the case of 953-His, two peaks were observed during gel filtration. The major peak (80%) represented a dimeric conformation of 953 while the minor peak (20%) had the expected size of a monomer. The monomeric form of 953 was found to have greater bactericidal activity than the dimer.

Example 5 - pSM214 and pET-24b vectors

[0140] 953 protein with its native leader peptide and no fusion partners was expressed from the pET vector and also from pSM214 [Velati Bellini et al. (1991) J. Biotechnol. 18, 177-192].

[0141] The 953 sequence was cloned as a full-length gene into pSM214 using the *E. coli* MM294-1 strain as a host. To do this, the entire DNA sequence of the 953 gene (from ATG to the STOP codon) was amplified by PCR using the following primers:

953L for/2 CCGGAATTCTTATGAAAAAAATCATCTTCGCCGC Eco RI

953L rev/2 GCCCAAGCTTTTATTGTTTGGCTGCCTCGATT Hind III

which contain *Eco*RI and *Hind*III restriction sites, respectively. The amplified fragment was digested with *Eco*RI and *Hind*III and ligated with the pSM214 vector digested with the same two enzymes. The ligated plasmid was transformed into *E.coli* MM294-1 cells (by incubation in ice for 65 minutes at 37° C) and bacterial cells plated on LB agar containing 20μg/ml of chloramphenicol.

[0142] Recombinant colonies were grown over-night at 37°C in 4 ml of LB broth containing 20 μg/ml of chloramphenicol; bacterial cells were centrifuged and plasmid DNA extracted as and analysed by restriction with *Eco*RI and *Hind*III. To analyse the ability of the recombinant colonies to express the protein, they were inoculated in LB broth containing 20μg/ml of chloramphenicol and let to grown for 16 hours at 37°C. Bacterial cells were centrifuged and resuspended in PBS. Expression of the protein was analysed by SDS-PAGE and Coomassie Blue staining.

[0143] Expression levels were unexpectedly high from the pSM214 plasmid.

[0144] Oligos used to clone sequences into pSM-214 vectors were as follows:

ΔG287	Fwd	CCGGAATTCTTATG-**T**CGCCCGATGTTAAATCGGCGGA	EcoRI
(pSM-214)	Rev	GCCCAAGCTT-**TCA**ATCCTGCTCTTTTTTGCCG	HindIII
Δ2 287	Fwd	CCGGAATTCTTATG-AGCCAAGATATGGCGGCAGT	EcoRI
(pSM-214)	Rev	GCCCAAGCTT-**TCAA**TCCTGCTCTTTTTTGCCG	HindIII
Δ3 287	Fwd	CCGGAATTCTTATG-TCCGCCGAATCCGCAAATCA	EcoRI
(pSM-214)	Rev	GCCCAAGCTT-**TCAA**TCCTGCTCTTTTTTGCCG	HindIII
Δ4 287	Fwd	CCGGAATTCTTATG-GGAAGGGTTGATTTGGCTAATG	EcoRI
(pSM-214)	Rev	GCCCAAGCTT-**TCAA**TCCTGCTCTTTTTTGCCG	HindIII
Orf46.1	Fwd	CCGGAATTCTTATG-TCAGATTTGGCAAACGATTCTT	EcoRI
(pSM-214)	Rev	GCCCAAGCTT-**TTA**CGTATCATATTTCACGTGCTTC	HindIII
ΔG287-Orf46.1	Fwd	CCGGAATTCTTATG-TCGCCCGATGTTAAATCGGCGGA	EcoRI
(pSM-214)	Rev	GCCCAAGCTT-**TTA**CGTATCATATTTCACGTGCTTC	HindIII
919	Fwd	CCGGAATTCTTATG-CAAAGCAAGAGCATCCAAACCT	EcoRI
(pSM-214)	Rev	GCCCAAGCTT-**TTA**CGGGCGGTATTCGGGCT	HindIII
961L	Fwd	CCGGAATTCATATG-AAACACTTTCCATCC	EcoRI
(pSM-214)	Rev	GCCCAAGCTT-**TTA**CCACTCGTAATTGAC	HindIII
961	Fwd	CCGGAATTCATATG-GCCACAAGCGACGAC	EcoRI
(pSM-214)	Rev	GCCCAAGCTT-**TTA**CCACTCGTAATTGAC	HindIII

(continued)

961c L	Fwd	CCGGAATTCTTATG-AAACACTTTCCATCC	EcoRI
pSM-214	Rev	GCCCAAGCTT-**TCAA**CCCACGTTGTAAGGTTG	HindIII
961c	Fwd	CCGGAATTCTTATG-GCCACAAACGACGACG	EcoRI
pSM-214	Rev	GCCCAAGCTT-**TCAA**CCCACGTTGTAAGGTTG	HindIII
953	Fwd	CCGGAATTCTTATG-GCCACCTACAAAGTGGACGA	EcoRI
(pSM-214)	Rev	GCCCAAGCTT-**TTA**TTGTTTGGCTGCCTCGATT	HindIII

These sequences were manipulated, cloned and expressed as described for 953L.

[0145] For the pET-24 vector, sequences were cloned and the proteins expressed in pET-24 as described below for pET21. pET2 has the same sequence as pET-21, but with the kanamycin resistance cassette instead of ampicillin cassette.

[0146] Oligonucleotides used to clone sequences into pET-24b vector were:

ΔG 287 K	Fwd	CGCGGATCCGCTAGC-CCCGATGTTAAATCGGC §	NheI
	Rev	CCCGCTCGAG-**TCA**ATCCTGCTCTTTTTTGCC *	XhoI
Δ2 287 K	Fwd	CGCGGATCCGCTAGC-CAAGATATGGCGGCAGT §	NheI
Δ3 287 K	Fwd	CGCGGATCCGCTAGC-GCCGAATCCGCAAATCA §	NheI
Δ4 287 K	Fwd	CGCGCTAGC-GGAAGGGTTGATTTGGCTAATGG §	NheI
Orf46.1 K	Fwd	GGGAATTCCATATG-GGCATTTCCCGCAAAATATC	NdeI
	Rev	CCCGCTCGAG-**TTA**CGTATCATATTTCACGTGC	XhoI
Orf46A K	Fwd	GGGAATTCCATATG-GGCATTTCCCGCAAAATATC	NdeI
	Rev	CCCGCTCGAG-**TTA**TTCTATGCCTTGTGCGGCAT	XhoI
961 K	Fwd	CGCGGATCCCATATG-GCCACAAGCGACGACGA	NdeI
(MC58)	Rev	CCCGCTCGAG-**TTA**CCACTCGTAATTGAC	XhoI
961a K	Fwd	CGCGGATCCCATATG-GCCACAAACGACG	NdeI
	Rev	CCCGCTCGAG-**TCA**TTTAGCAATATTATCTTTGTTC	XhoI
961b K	Fwd	CGCGGATCCCATATG-AAAGCAAACAGTGCCGAC	NdeI
	Rev	CCCGCTCGAG-**TTA**CCACTCGTAATTGAC	XhoI
961c K	Fwd	CGCGGATCCCATATG-GCCACAAACGACG	NdeI
	Rev	CCCGCTCGAG-**TTA**ACCCACGTTGTAAGGT	XhoI
961cL K	Fwd	CGCGGATCCCATATG-ATGAAACACTTTCCATCC	NdeI
	Rev	CCCGCTCGAG-**TTA**ACCCACGTTGTAAGGT	XhoI
961d K	Fwd	CGCGGATCCCATATG-GCCACAAACGACG	NdeI
	Rev	CCCGCTCGAG-**TCA**GTCTGACACTGTTTTATCC	XhoI
ΔG 287-	Fwd	CGCGGATCCGCTAGC-CCCGATGTTAAATCGGC	NheI
919 K	Rev	CCCGCTCGAG-**TTA**CGGGCGGTATTCGG	XhoI
ΔG 287-	Fwd	CGCGGATCCGCTAGC-CCCGATGTTAAATCGGC	NheI
Orf46.1 K	Rev	CCCGCTCGAG-**TTA**CGTATCATATTTCACGTGC	XhoI
ΔG 287-	Fwd	CGCGGATCCGCTAGC-CCCGATGTTAAATCGGC	NheI

(continued)

961 K	Rev	CCCGCTCGAG-**TTA**CCACTCGTAATTGAC	XhoI
* This primer was used as a Reverse primer for all the 287 forms. § Forward primers used in combination with the ΔG278 K reverse primer.			

Example 6 - ORF1 and its leader peptide

[0147] ORF1 from *N.meningitidis* (serogroup B, strain MC58) is predicted to be an outer membrane or secreted protein. It has the following sequence:

```
   1  MKTTDKRTTE THRKAPKTGR IRFSPAYLAI CLSFGILPQA WAGHTYFGIN
  51  YQYYRDFAEN KGKFAVGAKD IEVYNKKGEL VGKSMTKAPM IDFSVVSRNG
 101  VAALVGDQYI VSVAHNGGYN NVDFGAEGRN PDQHRFTYKI VKRNNYKAGT
 151  KGHPYGGDYH MPRLHKFVTD AEPVEMTSYM DGRKYIDQNN YPDRVRIGAG
 201  RQYWRSDEDE PNNRESSYHI ASAYSWLVGG NTFAQNGSGG GTVNLGSEKI
 251  KHSPYGFLPT GGSFGDSGSP MFIYDAQKQK WLINGVLQTG NPYIGKSNGF
 301  QLVRKDWFYD EIFAGDTHSV FYEPRQNGKY SFNDDNNGTG KINAKHEHNS
 351  LPNRLKTRTV QLFNVSLSET AREPVYHAAG GVNSYRPRLN NGENISFIDE
 401  GKGELILTSN INQGAGGLYF QGDFTVSPEN NETWQGAGVH ISEDSTVTWK
 451  VNGVANDRLS KIGKGTLHVQ AKGENQGSIS VGDGTVILDQ QADDKGKKQA
 501  FSEIGLVSGR GTVQLNADNQ FNPDKLYFGF RGGRLDLNGH SLSFHRIQNT
 551  DEGAMIVNHN QDKESTVTIT GNKDIATTGN NNSLDSKKEI AYNGWFGEKD
 601  TTKTNGRLNL VYQPAAEDRT LLLSGGTNLN GNITQTNGKL FFSGRPTPHA
 651  YNHLNDHWSQ KEGIPRGEIV WDNDWINRTF KAENFQIKGG QAVVSRNVAK
 701  VKGDWHLSNH AQAVFGVAPH QSHTICTRSD WTGLTNCVEK TITDDKVIAS
 751  LTKTDISGNV DLADHAHLNL TGLATLNGNL SANGDTRYTV SHNATQNGNL
 801  SLVGNAQATF NQATLNGNTS ASGNASFNLS DHAVQNGSLT LSGNAKANVS
 851  HSALNGNVSL ADKAVFHFES SRFTGQISGG KDTALHLKDS EWTLPSGTEL
 901  GNLNLDNATI TLNSAYRHDA AGAQTGSATD APRRRSRRSR RSLLSVTPPT
 951  SVESRFNTLT VNGKLNGQGT FRFMSELFGY RSDKLKLAES SEGTYTLAVN
1001  NTGNEPASLE QLTVVEGKDN KPLSENLNFT LQNEHVDAGA WRYQLIRKDG
1051  EFRLHNPVKE QELSDKLGKA EAKKQAEKDN AQSLDALIAA GRDAVEKTES
1101  VAEPARQAGG ENVGIMQAEE EKKRVQADKD TALAKQREAE TRPATTAFPR
1151  ARRARRDLPQ LQPQPQPQPQ RDLISRYANS GLSEFSATLN SVFAVQDELD
1201  RVFAEDRRNA VWTSGIRDTK HYRSQDFRAY RQQTDLRQIG MQKNLGSGRV
1251  GILFSHNRTE NTFDDGIGNS ARLAHGAVFG QYGIDRFYIG ISAGAGFSSG
1301  SLSDGIGGKI RRRVLHYGIQ ARYRAGFGGF GIEPHIGATR YFVQKADYRY
1351  ENVNIATPGL AFNRYRAGIK ADYSFKPAQH ISITPYLSLS YTDAASGKVR
1401  TRVNTAVLAQ DFGKTRSAEW GVNAEIKGFT LSLHAAAAKG PQLEAQHSAG
1451  IKLGYRW*
```

The leader peptide is underlined.

[0148] A polymorphic form of ORF1 is disclosed in WO99/55873.

[0149] Three expression strategies have been used for ORF1:

1) ORF1 using a His tag, following WO99/24578 (ORF1-His);
2) ORF1 with its own leader peptide but without any fusion partner ('ORF1L'); and
3) ORF1 with the leader peptide (MKKTAIAIAVALAGFATVAQA) from *E.coli* OmpA ('Orf1LOmpA'):

```
MKKTAIAIAVALAGFATVAQAASAGHTYFGINYQYYRDFAENKGKFAVGAKDIEVYNKKGELVGKSMTKAPMIDFSV
VSRNGVAALVGDQYIVSVAHNGGYNNVDFGAEGRNPDQHRFTYKIVKRNNYKAGTKGHPYGGDYHMPRLHKFVTDAE
PVEMTSYMDGRKYIDQNNYPDRVRIGAGRQYWRSDEDEPNNRESSYHIASAYSWLVGGNTFAQNGSGGGTVNLGSEK
IKHSPYGFLPTGGSFGDSGSPMFIYDAQKQKWLINGVLQTGNPYIGKSNGFQLVRKDWFYDEIFAGDTHSVFYEPRQ
NGKYSFNDDNNGTGKINAKHEHNSLPNRLKTRTVQLFNVSLSETAREPVYHAAGGVNSYRPRLNNGENISFIDEGKG
ELILTSNINQGAGGLYFQGDFTVSPENNETWQGAGVHISEDSTVTWKVNGVANDRLSKIGKGTLHVQAKGENQGSIS
VGDGTVILDQQADDKGKKQAFSEIGLVSGRGTVQLNADNQFNPDKLYFGFRGGRLDLNGHSLSFHRIQNTDEGAMIV
NHNQDKESTVTITGNKDIATTGNNNSLDSKKEIAYNGWFGEKDTTKTNGRLNLVYQPAAEDRTLLLSGGTNLNGNIT
QTNGKLFFSGRPTPHAYNHLNDHWSQKEGIPRGEIVWDNDWINRTFKAENFQIKGGQAVVSRNVAKVKGDWHLSNHA
QAVFGVAPHQSHTICTRSDWTGLTNCVEKTITDDKVIASLTKTDISGNVDLADHAHLNLTGLATLNGNLSANGDTRY
TVSHNATQNGNLSLVGNAQATFNQATLNGNTSASGNASFNLSDHAVQNGSLTLSGNAKANVSHSALNGNVSLADKAV
FHFESSRFTGQISGGKDTALHLKDSEWTLPSGTELGNLNLDNATITLNSAYRHDAAGAQTGSATDAPRRRSRRSRRS
LLSVTPPTSVESRFNTLTVNGKLNGQGTFRFMSELFGYRSDKLKLAESSEGTYTLAVNNTGNEPASLEQLTVVEGKD
NKPLSENLNFTLQNEHVDAGAWRYQLIRKDGEFRLHNPVKEQELSDKLGKAEAKKQAEKDNAQSLDALIAAGRDAVE
KTESVAEPARQAGGENVGIMQAEEEKKRVQADKDTALAKQREAETRPATTAFPRARRARRDLPQLQPQPQPQPQRDL
ISRYANSGLSEFSATLNSVFAVQDELDRVFAEDRRNAVWTSGIRDTKHYRSQDFRAYRQQTDLRQIGMQKNLGSGRV
GILFSHNRTENTFDDGIGNSARLAHGAVFGQYGIDRFYIGISAGAGFSSGSLSDGIGGKIRRRVLHYGIQARYRAGF
GGFGIEPHIGATRYFVQKADYRYENVNIATPGLAFNRYRAGIKADYSFKPAQHISITPYLSLSYTDAASGKVRTRVN
TAVLAQDFGKTRSAEWGVNAEIKGFTLSLHAAAAKGPQLEAQHSAGIKLGYRW*
```

To make this construct, the clone pET911 LOmpA (see below) was digested with the *Nhe*I and *Xho*I restriction enzymes and the fragment corresponding to the vector carrying the OmpA leader sequence was purified (pETLOmpA). The ORF1 gene coding for the mature protein was amplified using the oligonucleotides ORF1-For and ORF1-Rev (including the *Nhe*I and *Xho*I restriction sites, respectively), digested with *Nhe*I and *Xho*I and ligated to the purified pETOmpA fragment (see Figure 1). An additional AS dipeptide was introduced by the *Nhe*I site.

[0150] All three forms of the protein were expressed. The His-tagged protein could be purified and was confirmed as surface exposed, and possibly secreted (see Figure 3). The protein was used to immunise mice, and the resulting sera gave excellent results in the bactericidal assay.

[0151] ORF1LOmpA was purified as total membranes, and was localised in both the inner and outer membranes. Unexpectedly, sera raised against ORF1LOmpA show even better ELISA and anti-bactericidal properties than those raised against the His-tagged protein.

[0152] ORF1L was purified as outer membranes, where it is localised.

Example 7 - protein 911 and its leader peptide

[0153] Protein 911 from *N.meningitidis* (serogroup B, strain MC58) has the following sequence:

```
  1  MKKNILEFWV GLFVLIGAAA VAFLAFRVAG GAAFGGSDKT YAVYADFGDI
 51  GGLKVNAPVK SAGVLVGRVG AIGLDPKSYQ ARVRLDLDGK YQFSSDVSAQ
101  ILTSGLLGEQ YIGLQQGGDT ENLAAGDTIS VTSSAMVLEN LIGKFMTSFA
151  EKNADGGNAE KAAE*
```

The leader peptide is underlined.

[0154] Three expression strategies have been used for 911:

1) 911 with its own leader peptide but without any fusion partner ('911L');

2) 911 with the leader peptide from *E.coli* OmpA ('911LOmpA'). To make this construct, the entire sequence encoding the OmpA leader peptide was included in the 5'- primer as a tail (primer 911LOmpA Forward). A *Nhe*I restriction site was inserted between the sequence coding for the OmpA leader peptide and the 911 gene encoding the predicted mature protein (insertion of one amino acid, a serine), to allow the use of this construct to clone different genes downstream the OmpA leader peptide sequence.

3) 911 with the leader peptide (MKYLLPTAAAGLLLAAQPAMA) from *Erwinia carotovora* PelB ('911LpelB').

[0155] To make this construct, the 5'-end PCR primer was designed downstream from the leader sequence and included the *Nco*I restriction site in order to have the 911 fused directly to the PelB leader sequence; the 3'- end primer included the STOP codon. The expression vector used was pET22b+ (Novagen), which carries the coding sequence

for the PelB leader peptide. The *Nco*I site introduces an additional methionine after the PelB sequence.

[0156] All three forms of the protein were expressed. ELISA titres were highest using 911 L, with 919LOmpA also giving good results.

Example 8 - ORF46

[0157] The complete ORF46 protein from *N.meningitidis* (serogroup B, strain 2996) has the following sequence:

```
  1 LGISRKISLI LSILAVCLPM HAHASDLAND SFIRQVLDRQ HFEPDGKYHL
 51 FGSRGELAER SGHIGLGKIQ SHQLGNLMIQ QAAIKGNIGY IVRFSDHGHE
101 VHSPFDNHAS HSDSDEAGSP VDGFSLYRIH WDGYEHHPAD GYDGPQGGGY
151 PAPKGARDIY SYDIKGVAQN IRLNLTDNRS TGQRLADRFH NAGSMLTQGV
201 GDGFKRATRY SPELDRSGNA AEAFNGTADI VKNIIGAAGE IVGAGDAVQG
251 ISEGSNIAVM HGLGLLSTEN KMARINDLAD MAQLKDYAAA AIRDWAVQNP
301 NAAQGIEAVS NIFMAAIPIK GIGAVRGKYG LGGITAHPIK RSQMGAIALP
351 KGKSAVSDNF ADAAYAKYPS PYHSRNIRSN LEQRYGKENI TSSTVPPSNG
401 KNVKLADQRH PKTGVPFDGK GFPNFEKHVK YDTKLDIQEL SGGGIPKAKP
451 VSDAKPRWEV DRKLNKLTTR EQVEKNVQEI RNGNKNSNFS QHAQLEREIN
501 KLKSADEINF ADGMGKFTDS MNDKAFSRLV KSVKENGFTN PVVEYVEING
551 KAYIVRGNNR VFAAEYLGRI HELKFKKVDF PVPNTSWKNP TDVLNESGNV
601 KRPRYRSK*
```

The leader peptide is underlined.

[0158] The sequences of ORF46 from other strains can be found in WO00/66741.

[0159] Three expression strategies have been used for ORF46:

1) ORF46 with its own leader peptide but without any fusion partner ('ORF46-2L');
2) ORF46 without its leader peptide and without any fusion partner ('ORF46-2'), with the leader peptide omitted by designing the 5'-end amplification primer downstream from the predicted leader sequence:

```
  1 SDLANDSFIR QVLDRQHFEP DGKYHLFGSR GELAERSGHI GLGKIQSHQL
 51 GNLMIQQAAI KGNIGYIVRF SDHGHEVHSP FDNHASHSDS DEAGSPVDGF
101 SLYRIHWDGY EHHPADGYDG PQGGGYPAPK GARDIYSYDI KGVAQNIRLN
151 LTDNRSTGQR LADRFHNAGS MLTQGVGDGF KRATRYSPEL DRSGNAAEAF
201 NGTADIVKNI IGAAGEIVGA GDAVQGISEG SNIAVMHGLG LLSTENKMAR
251 INDLADMAQL KDYAAAAIRD WAVQNPNAAQ GIEAVSNIFM AAIPIKGIGA
301 VRGKYGLGGI TAHPIKRSQM GAIALPKGKS AVSDNFADAA YAKYPSPYHS
351 RNIRSNLEQR YGKENITSST VPPSNGKNVK LADQRHPKTG VPFDGKGFPN
401 FEKHVKYDTK LDIQELSGGG IPKAKPVSDA KPRWEVDRKL NKLTTREQVE
451 KNVQEIRNGN KNSNFSQHAQ LEREINKLKS ADEINFADGM GKFTDSMNDK
501 AFSRLVKSVK ENGFTNPVVE YVEINGKAYI VRGNNRVFAA EYLGRIHELK
551 FKKVDFPVPN TSWKNPTDVL NESGNVKRPR YRSK*
```

3) ORF46 as a truncated protein, consisting of the first 433 amino acids ('ORF46.1L'), constructed by designing PCR primers to amplify a partial sequence corresponding to aa 1-433.
A STOP codon was included in the 3'-end primer sequences.

[0160] ORF46-2L is expressed at a very low level to *E. coli.* Removal of its leader peptide (ORF46-2) does not solve this problem. The truncated ORF46.1L form (first 433 amino acids, which are well conserved between serogroups and species), however, is well-expressed and gives excellent results in ELISA test and in the bactericidal assay.

[0161] ORF46.1 has also been used as the basis of hybrid proteins. It has been fused with 287, 919, and ORF1. The hybrid proteins were generally insoluble, but gave some good ELISA and bactericidal results (against the homologous 2996 strain):

Protein	ELISA	Bactericidal Ab
Orf1-Orf46.1-His	850	256

(continued)

Protein	ELISA	Bactericidal Ab
919-Orf46.1-His	12900	512
919-287-Orf46-His	n.d.	n.d.
Orf46.1-287His	150	8192
Orf46.1-919His	2800	2048
Orf46.1-287-919His	3200	16384

[0162] For comparison, 'triple' hybrids of ORF46.1, 287 (either as a GST fusion, or in ΔG287 form) and 919 were constructed and tested against various strains (including the homologous 2996 strain) *versus* a simple mixture of the three antigens. FCA was used as adjuvant:

	2996	BZ232	MC58	NGH38	F6124	BZ133
Mixture	8192	256	512	1024	>2048	>2048
ORF46.1-287-919his	16384	256	4096	8192	8192	8192
ΔG287-919-ORF46.1his	8192	64	4096	8192	8192	16384
ΔG287-ORF46.1-919his	4096	128	256	8192	512	1024

Again, the hybrids show equivalent or superior immunological activity.

[0163] Hybrids of two proteins (strain 2996) were compared to the individual proteins against various heterologous strains:

	1000	MC58	F6124 (MenA)
ORF46.1-His	<4	4096	<4
ORF1-His	8	256	128
ORF1—ORF46.1-His	1024	512	1024

[0164] Again, the hybrid shows equivalent or superior immunological activity.

Example 9 - protein 961

[0165] The complete 961 protein from *N.meningitidis* (serogroup B, strain MC58) has the following sequence:

```
  1 MSMKHFPAKV LTTAILATFC SGALAATSDD DVKKAATVAI VAAYNNGQEI
 51 NGFKAGETIY DIGEDGTITQ KDATAADVEA DDFKGLGLKK VVTNLTKTVN
101 ENKQNVDAKV KAAESEIEKL TTKLADTDAA LADTDAALDE TTNALNKLGE
151 NITTFAEETK TNIVKIDEKL EAVADTVDKH AEAFNDIADS LDETNTKADE
201 AVKTANEAKQ TAEETKQNVD AKVKAAETAA GKAEAAAGTA NTAADKAEAV
251 AAKVTDIKAD IATNKADIAK NSARIDSLDK NVANLRKETR QGLAEQAALS
301 GLFQPYNVGR FNVTAAVGGY KSESAVAIGT GFRFTENFAA KAGVAVGTSS
351 GSSAAYHVGV NYEW*
```

[0166] The leader peptide is underlined.

[0167] Three approaches to 961 expression were used:

1) 961 using a GST fusion, following WO99/57280 ('GST961');
2) 961 with its own leader peptide but without any fusion partner ('961L'); and
3) 961 without its leader peptide and without any fusion partner ('961^{untagged}'), with the leader peptide omitted by

designing the 5'-end PCR primer downstream from the predicted leader sequence.

[0168] All three forms of the protein were expressed. The GST-fusion protein could be purified and antibodies against it confirmed that 961 is surface exposed (Figure 4). The protein was used to immunise mice, and the resulting sera gave excellent results in the bactericidal assay. 961 L could also be purified and gave very high ELISA titres.
[0169] Protein 961 appears to be phase variable. Furthermore, it is not found in all strains of *N.meningitidis.*

Example 10 - protein 287

[0170] Protein 287 from *N.meningitidis* (serogroup B, strain 2996) has the following sequence:

```
  1  MFERSVIAMA CIFALSACGG GGGGSPDVKS ADTLSKPAAP VVAEKETEVK
 51  EDAPQAGSQG QGAPSTQGSQ DMAAVSAENT GNGGAATTDK PKNEDEGPQN
101  DMPQNSAESA NQTGNNQPAD SSDSAPASNP APANGGSNFG RVDLANGVLI
151  DGPSQNITLT HCKGDSCNGD NLLDEEAPSK SEFENLNESE RIEKYKKDGK

201  SDKFTNLVAT AVQANGTNKY VIIYKDKSAS SSSARFRRSA RSRRSLPAEM
251  PLIPVNQADT LIVDGEAVSL TGHSGNIFAP EGNYRYLTYG AEKLPGGSYA
301  LRVQGEPAKG EMLAGTAVYN GEVLHFHTEN GRPYPTRGRF AAKVDFGSKS
351  VDGIIDSGDD LHMGTQKFKA AIDGNGFKGT WTENGGGDVS GRFYGPAGEE
401  VAGKYSYRPT DAEKGGFGVF AGKKEQD*
```

[0171] The leader peptide is shown underlined.
[0172] The sequences of 287 from other strains can be found in Figures 5 and 15 of WO00/66741.
[0173] Example 9 of WO99/57280 discloses the expression of 287 as a GST-fusion in *E.coli.*
[0174] A number of further approaches to expressing 287 in *E.coli* have been used, including:

1) 287 as a His-tagged fusion ('287-His');
2) 287 with its own leader peptide but without any fusion partner ('287L');
3) 287 with the ORF4 leader peptide and without any fusion partner ('287LOrf4'); and
4) 287 without its leader peptide and without any fusion partner ('287^{untagged}'):

```
  1  CGGGGGGSPD VKSADTLSKP AAPVVAEKET EVKEDAPQAG SQGQGAPSTQ
 51  GSQDMAAVSA ENTGNGGAAT TDKPKNEDEG PQNDMPQNSA ESANQTGNNQ
101  PADSSDSAPA SNPAPANGGS NFGRVDLANG VLIDGPSQNI TLTHCKGDSC
151  NGDNLLDEEA PSKSEFENLN ESERIEKYKK DGKSDKFTNL VATAVQANGT
201  NKYVIIYKDK SASSSSARFR RSARSRRSLP AEMPLIPVNQ ADTLIVDGEA
251  VSLTGHSGNI FAPEGNYRYL TYGAEKLPGG SYALRVQGEP AKGEMLAGTA
301  VYNGEVLHFH TENGRPYPTR GRFAAKVDFG SKSVDGIIDS GDDLHMGTQK
351  FKAAIDGNGF KGTWTENGGG DVSGRFYGPA GEEVAGKYSY RPTDAEKGGF
401  GVFAGKKEQD *
```

[0175] All these proteins could be expressed and purified.
[0176] '287L' and '287LOrf4' were confirmed as lipoproteins.
[0177] As shown in Figure 2, '287LOrf4' was constructed by digesting 919LOrf4 with *Nhe*I and *Xho*I. The entire ORF4 leader peptide was restored by the addition of a DNA sequence coding for the missing amino acids, as a tail, in the 5'-end primer (287LOrf4 for), fused to 287 coding sequence. The 287 gene coding for the mature protein was amplified using the oligonucleotides 287LOrf4 For and Rev (including the *Nhe*I and *Xho*I sites, respectively), digested with *Nhe*I and *Xho*I and ligated to the purified pETOrf4 fragment.

Example 11 - further non-fusion proteins with/without native leader peptides

[0178] A similar approach was adopted for *E.coli* expression of further proteins from WO99/24578, WO99/36544 and WO99/57280.

[0179] The following were expressed without a fusion partner: 008, 105, 117-1, 121-1, 122-1, 128-1, 148, 216, 243, 308, 593, 652, 726, 982, and Orf143-1. Protein 117-1 was confirmed as surface-exposed by FACS and gave high ELISA titres.

[0180] The following were expressed with the native leader peptide but without a fusion partner: 111, 149, 206, 225-1, 235, 247-1, 274, 283, 286, 292, 401, 406, 502-1, 503, 519-1, 525-1, 552, 556, 557, 570, 576-1, 580, 583, 664, 759, 907, 913, 920-1, 926, 936-1, 953, 961, 983, 989, Orf4, Orf7-1, Orf9-1, Orf23, Orf25, Orf37, Orf38, Orf40, Orf40.1, Orf40.2, Orf72-1, Orf76-1, Orf85-2, Orf91, Orf97-1, Orf119, Orf143.1. These proteins are given the suffix 'L'.

[0181] His-tagged protein 760 was expressed with and without its leader peptide. The deletion of the signal peptide greatly increased expression levels. The protein could be purified most easily using 2M urea for solubilisation.

[0182] His-tagged protein 264 was well-expressed using its own signal peptide, and the 30kDa protein gave positive Western blot results.

[0183] All proteins were successfully expressed.

[0184] The localisation of 593, 121-1, 128-1, 593, 726, and 982 in the cytoplasm was confirmed.

[0185] The localisation of 920-1L, 953L, ORF9-1L, ORF85-2L, ORF97-1L, 570L, 580L and 664L in the periplasm was confirmed.

[0186] The localisation of ORF40L in the outer membrane, and 008 and 519-1L in the inner membrane was confirmed. ORF25L, ORF4L, 406L, 576-1L were all confirmed as being localised in the membrane.

[0187] Protein 206 was found not to be a lipoprotein.

[0188] ORF25 and ORF40 expressed with their native leader peptides but without fusion partners, and protein 593 expressed without its native leader peptide and without a fusion partner, raised good anti-bactericidal sera. Surprisingly, the forms of ORF25 and ORF40 expressed without fusion partners and using their own leader peptides (i.e. 'ORF25L' and 'ORF40L') give better results in the bactericidal assay than the fusion proteins.

[0189] Proteins 920L and 953L were subjected to N-terminal sequencing, giving HRVWVETAH and ATYKVDEY-HANARFAF, respectively. This sequencing confirms that the predicted leader peptides were cleaved and, when combined with the periplasmic location, confirms that the proteins are correctly processed and localised by *E.coli* when expressed from their native leader peptides.

[0190] The N-terminal sequence of protein 519.1L localised in the inner membrane was MEFFIILLA, indicating that the leader sequence is not cleaved. It may therefore function as both an uncleaved leader sequence and a transmembrane anchor in a manner similar to the leader peptide of PBP1 from *N.gonorrhoeae* [Ropp & Nicholas (1997) J. Bact. 179: 2783-2787.]. Indeed the N-terminal region exhibits strong hydrophobic character and is predicted by the Tmpred. program to be transmembrane.

Example 12 - lipoproteins

[0191] The incorporation of palmitate in recombinant lipoproteins was demonstrated by the method of Kraft et. al. [J. Bact. (1998) 180:3441-3447.]. Single colonies harbouring the plasmid of interest were grown overnight at 37°C in 20 ml of LB/Amp (100μg/ml) liquid culture. The culture was diluted to an OD_{550} of 0.1 in 5.0 ml of fresh medium LB/Amp medium containing 5 μC/ml [^{3}H] palmitate (Amersham). When the OD_{550} of the culture reached 0.4-0.8, recombinant lipoprotein was induced for 1 hour with IPTG (final concentration 1.0 mM). Bacteria were harvested by centrifugation in a bench top centrifuge at 2700g for 15 min and washed twice with 1.0 ml cold PBS. Cells were resuspended in 120μl of 20 mM Tris-HCl (pH 8.0), 1 mM EDTA, 1.0% w/v SDS and lysed by boiling for 10 min. After centrifugation at 13000g for 10 min the supernatant was collected and proteins precipitated by the addition of 1.2 ml cold acetone and left for 1 hour at -20 °C. Protein was pelleted by centrifugation at 13000g for 10 min and resuspended in 20-50μl (calculated to standardise loading with respect to the final O.D of the culture) of 1.0% w/v SDS. An aliquot of 15 μl was boiled with 5μl of SDS-PAGE sample buffer and analysed by SDS-PAGE. After electrophoresis gels were fixed for 1 hour in 10% v/v acetic acid and soaked for 30 minutes in Amplify solution (Amersham). The gel was vacuum-dried under heat and exposed to Hyperfilm (Kodak) overnight -80 °C.

[0192] Incorporation of the [^{3}H] palmitate label, confirming lipidation, was found for the following proteins: Orf4L, Orf25L, 287L, 287LOrf4, 406.L, 576L, 926L, 919L and 919LOrf4.

Example 13 - domains in 287

[0193] Based on homology of different regions of 287 to proteins that belong to different functional classes, it was split into three 'domains', as shown in Figure 5. The second domain shows homology to IgA proteases, and the third domain shows homology to transferrin-binding proteins.

[0194] Each of the three 'domains' shows a different degree of sequence conservation between *N.meningitidis* strains - domain C is 98% identical, domain A is 83% identical, whilst domain B is only 71% identical. Note that protein 287 in strain MC58 is 61 amino acids longer than that of strain 2996. An alignment of the two sequences is shown in Figure

7, and alignments for various strains are disclosed in WO00/66741 (see Figures 5 and 15 therein).

[0195] The three domains were expressed individually as C-terminal His-tagged proteins. This was done for the MC58 and 2996 strains, using the following constructs:

287a-MC58 (aa 1-202), 287b-MC58 (aa 203-288), 287c-MC58 (aa 311-488).

287a-2996 (aa 1-139), 287b-2996 (aa 140-225), 287c-2996 (aa 250-427).

[0196] To make these constructs, the stop codon sequence was omitted in the 3'-end primer sequence. The 5' primers included the *Nhe*I restriction site, and the 3' primers included a *Xho*I as a tail, in order to direct the cloning of each amplified fragment into the expression vector pET21 b+ using *Nde*I-*Xho*I, *Nhe*I-*Xho*I or *Nde*I-*Hind*III restriction sites.

[0197] All six constructs could be expressed, but 287b-MC8 required denaturation and refolding for solubilisation.

[0198] Deletion of domain A is described below ('Δ4 287-His').

[0199] Immunological data (serum bactericidal assay) were also obtained using the various domains from strain 2996, against the homologous and heterologous MenB strains, as well as MenA (F6124 strain) and MenC (BZ133 strain):

	2996	BZ232	MC58	NGH38	394/98	MenA	MenC
287-His	32000	16	4096	4096	512	8000	16000
287(B)-His	256	-	-	-	-	16	-
287(C)-His	256	-	32	512	32	2048	>2048
287(B-C)-His	64000	128	4096	64000	1024	64000	32000

[0200] Using the domains of strain MC58, the following results were obtained:

	MC58	2996	BZ232	NGH38	394/98	MenA	MenC
287-His	4096	32000	16	4096	512	8000	16000
287(B)-His	128	128	-	-	-	-	128
287(C)-His	-	16	-	1024	-	512	-
287(B-C)-His	16000	64000	128	64000	512	64000	>8000

Example 14 — deletions in 287

[0201] As well as expressing individual domains, 287 was also expressed (as a C-terminal His-tagged protein) by making progressive deletions within the first domain. These

[0202] Four deletion mutants of protein 287 from strain 2996 were used (Figure 6):

1) '287-His', consisting of amino acids 18-427 (*i.e.* leader peptide deleted);
2) 'Δ1 287-His', consisting of amino acids 26-427;
3) 'Δ2 287-His', consisting of amino acids 70-427;
4) 'Δ3 287-His', consisting of amino acids 107-427; and
5) 'Δ4 287-His', consisting of amino acids 140-427 (=287-bc).

[0203] The 'Δ4' protein was also made for strain MC58 ('Δ4 287MC58-His'; aa 203-488).

[0204] The constructs were made in the same way as 287a/b/c, as described above.

[0205] All six constructs could be expressed and protein could be purified. Expression of 287-His was, however, quite poor.

[0206] Expression was also high when the C-terminal His-tags were omitted.

[0207] Immunological data (serum bactericidal assay) were also obtained using the deletion mutants, against the homologous (2996) and heterologous MenB strains, as well as MenA (F6124 strain) and MenC (BZ133 strain):

	2996	BZ232	MC58	NGH38	394/98	MenA	MenC
287-his	32000	16	4096	4096	512	8000	16000
Δ1 287-His	16000	128	4096	4096	1024	8000	16000
Δ2 287-His	16000	128	4096	>2048	512	16000	>8000

(continued)

	2996	BZ232	MC58	NGH38	394/98	MenA	MenC
Δ3 287-His	16000	128	4096	>2048	512	16000	>8000
Δ4 287-His	64000	128	4096	64000	1024	64000	32000

[0208] The same high activity for the Δ4 deletion was seen using the sequence from strain MC58.

[0209] As well as showing superior expression characteristics, therefore, the mutants are immunologically equivalent or superior.

Example 15 - poly-glycine deletions

[0210] The 'Δ1 287-His' construct of the previous example differs from 287-His and from '287 untagged' only by a short N-terminal deletion (GGGGGGS). Using an expression vector which replaces the deleted serine with a codon present in the *Nhe* cloning site, however, this amounts to a deletion only of $(Gly)_6$. Thus, the deletion of this $(Gly)_6$ sequence has been shown to have a dramatic effect on protein expression.

[0211] The protein lacking the N-terminal amino acids up to GGGGGG is called 'ΔG 287'. In strain MC58, its sequence (leader peptide underlined) is:

```
                                    ΔG287
  1  MFKRSVIAMA CIFALSACGG GGGGSPDVKS ADTLSKPAAP VVSEKETEAK
 51  EDAPQAGSQG QGAPSAQGSQ DMAAVSEENT GNGGAVTADN PKNEDEVAQN
101  DMPQNAAGTD SSTPNHTPDP NMLAGNMENQ ATDAGESSQP ANQPDMANAA
151  DGMQGDDPSA GGQNAGNTAA QGANQAGNNQ AAGSSDPIPA SNPAPANGGS
201  NFGRVDLANG VLIDGPSQNI TLTHCKGDSC SGNNFLDEEV QLKSEFEKLS
251  DADKISNYKK DGKNDKFVGL VADSVQMKGI NQYIIFYKPK PTSFARFRRS
301  ARSRRSLPAE MPLIPVNQAD TLIVDGEAVS LTGHSGNIFA PEGNYRYLTY
351  GAEKLPGGSY ALRVQGEPAK GEMLAGAAVY NGEVLHFHTE NGRPYPTRGR
401  FAAKVDFGSK SVDGIIDSGD DLHMGTQKFK AAIDGNGFKG TWTENGSGDV
451  SGKFYGPAGE EVAGKYSYRP TDAEKGGFGV FAGKKEQD*
```

[0212] ΔG287, with or without His-tag ('ΔG287-His' and 'ΔG287K', respectively), are expressed at very good levels in comparison with the '287-His' or '287 untagged'.

[0213] On the basis of gene variability data, variants of ΔG287-His were expressed in *E.coli* from a number of MenB strains, in particular from strains 2996, MC58, 1000, and BZ232. The results were also good.

[0214] It was hypothesised that poly-Gly deletion might be a general strategy to improve expression. Other MenB lipoproteins containing similar $(Gly)_n$ motifs (near the N-terminus, downstream of a cysteine) were therefore identified, namely Tbp2 (NMB0460), 741 (NMB 1870) and 983 (NMB1969):

```
TBP2                                  ΔGTbp2
  1  MNNPLVNQAA MVLPVFLLSA CLGGGGSFDL DSVDTEAPRP APKYQDVFSE
 51  KPQAQKDQGG YGFAMRLKRR NWYPQAKEDE VKLDESDWEA TGLPDEPKEL
101  PKRQKSVIEK VETDSDNNIY SSPYLKPSNH QNGNTGNGIN QPKNQAKDYE
151  NFKYVYSGWF YKHAKREFNL KVEPKSAKNG DDGYIFYHGK EPSRQLPASG
201  KITYKGVWHF ATDTKKGQKF REIIQPSKSQ GDRYSGFSGD DGEEYSNKNK
251  STLTDGQEGY GFTSNLEVDF HNKKLTGKLI RNNANTDNNQ ATTTQYYSLE
301  AQVTGNRFNG KATATDKPQQ NSETKEHPFV SDSSSLSGGF FGPQGEELGF
351  RFLSDDQKVA VVGSAKTKDK PANGNTAAAS GGTDAAASNG AAGTSSENGK
401  LTTVLDAVEL KLGDKEVQKL DNFSNAAQLV VDGIMIPLLP EASESGNNQA
```

```
451  NQGTNGGTAF TRKFDHTPES DKKDAQAGTQ TNGAQTASNT AGDTNGKTKT
501  YEVEVCCSNL NYLKYGMLTR KNSKSAMQAG ESSSQADAKT EQVEQSMFLQ
551  GERTDEKEIP SEQNIVYRGS WYGYIANDKS TSWSGNASNA TSGNRAEFTV
601  NFADKKITGT LTADNRQEAT FTIDGNIKDN GFEGTAKTAE SGFDLDQSNT
651  TRTPKAYITD AKVQGGFYGP KAEELGGWFA YPGDKQTKNA TNASGNSSAT
701  VVFGAKRQQP VR*
```

741

```
                                ( ΔG741
  1  VNRTAFCCLS LTTALILTAC SSGGGGVAAD IGAGLADALT APLDHKDKGL
 51  QSLTLDQSVR KNEKLKLAAQ GAEKTYGNGD SLNTGKLKND KVSRFDFIRQ
101  IEVDGQLITL ESGEFQVYKQ SHSALTAFQT EQIQDSEHSG KMVAKRQFRI
151  GDIAGEHTSF DKLPEGGRAT YRGTAFGSDD AGGKLTYTID FAAKQGNGKI
201  EHLKSPELNV DLAAADIKPD GKRHAVISGS VLYNQAEKGS YSLGIFGGKA
251  QEVAGSAEVK TVNGIRHIGL AAKQ*
```

983

```
                                           ( ΔG983
   1  MRTTPTFPTK TFKPTAMALA VATTLSACLG GGGGGTSAPD FNAGGTGIGS
  51  NSRATTAKSA AVSYAGIKNE MCKDRSMLCA GRDDVAVTDR DAKINAPPPN
 101  LHTGDFPNPN DAYKNLINLK PAIEAGYTGR GVEVGIVDTG ESVGSISFPE
 151  LYGRKEHGYN ENYKNYTAYM RKEAPEDGGG KDIEASFDDE AVIETEAKPT
 201  DIRHVKEIGH IDLVSHIIGG RSVDGRPAGG IAPDATLHIM NTNDETKNEM
 251  MVAAIRNAWV KLGERGVRIV NNSFGTTSRA GTADLFQIAN SEEQYRQALL
 301  DYSGGDKTDE GIRLMQQSDY GNLSYHIRNK NMLFIFSTGN DAQAQPNTYA
 351  LLPFYEKDAQ KGIITVAGVD RSGEKFKREM YGEPGTEPLE YGSNHCGITA
 401  MWCLSAPYEA SVRFTRTNPI QIAGTSFSAP IVTGTAALLL QKYPWMSNDN
 451  LRTTLLTTAQ DIGAVGVDSK FGWGLLDAGK AMNGPASFPF GDFTADTKGT
 501  SDIAYSFRND ISGTGGLIKK GGSQLQLHGN NTYTGKTIIE GGSLVLYGNN
 551  KSDMRVETKG ALIYNGAASG GSLNSDGIVY LADTDQSGAN ETVHIKGSLQ
 601  LDGKGTLYTR LGKLLKVDGT AIIGGKLYMS ARGKGAGYLN STGRRVPFLS
 651  AAKIGQDYSF FTNIETDGGL LASLDSVEKT AGSEGDTLSY YVRRGNAART
 701  ASAAAHSAPA GLKHAVEQGG SNLENLMVEL DASESSATPE TVETAAADRT
 751  DMPGIRPYGA TFRAAAAVQH ANAADGVRIF NSLAATVYAD STAAHADMQG
 801  RRLKAVSDGL DHNGTGLRVI AQTQQDGGTW EQGGVEGKMR GSTQTVGIAA
 851  KTGENTTAAA TLGMGRSTWS ENSANAKTDS ISLFAGIRHD AGDIGYLKGL
 901  FSYGRYKNSI SRSTGADEHA EGSVNGTLMQ LGALGGVNVP FAATGDLTVE
 951  GGLRYDLLKQ DAFAEKGSAL GWSGNSLTEG TLVGLAGLKL SQPLSDKAVL
1001  FATAGVERDL NGRDYTVTGG FTGATAATGK TGARNMPHTR LVAGLGADVE
1051  FGNGWNGLAR YSYAGSKQYG NHSGRVGVGY RF*
```

[0215] Tbp2 and 741 genes were from strain MC58; 983 and 287 genes were from strain 2996. These were cloned in pET vector and expressed in *E.coli* without the sequence coding for their leader peptides or as "ΔG forms", both fused to a C-terminal His-tag. In each case, the same effect was seen - expression was good in the clones carrying the deletion of the poly-glycine stretch, and poor or absent if the glycines were present in the expressed protein:

ORF	Express.	Purification	Bact. Activity
287-His(2996)	+/-	+	+
'$287^{untagged}$'(2996)	+/-	nd	nd
ΔG287-His(2996)	+	+	+
ΔG287K(2996)	+	+	+
ΔG287-His(MC58)	+	+	+
ΔG287-His(1000)	+	+	+
ΔG287-His(BZ232)	+	+	+
Tbp2-His(MC58)	+/-	nd	nd
ΔGTbp2-His(MC58)	+	+	
741-His(MC58)	+/-	nd	nd

(continued)

ORF	Express.	Purification	Bact. Activity
ΔG741-His(MC58)	+	+	
983-His (2996)			
ΔG983-His (2996)	+	+	

[0216] SDS-PAGE of the proteins is shown in Figure 13.

ΔG287 and hybrids

[0217] ΔG287 proteins were made and purified for strains MC58, 1000 and BZ232. Each of these gave high ELISA titres and also serum bactericidal titres of>8192. ΔG287K, expressed from pET-24b, gave excellent titres in ELISA and the serum bactericidal assay. ΔG287-ORF46.1K may also be expressed in pET-24b.

[0218] ΔG287 was also fused directly in-frame upstream of 919, 953, 961 (sequences shown below) and ORF46.1:

<u>ΔG287–919</u>

```
   1  ATGGCTAGCC CCGATGTTAA ATCGGCGGAC ACGCTGTCAA AACCGGCCGC
  51  TCCTGTTGTT GCTGAAAAAG AGACAGAGGT AAAAGAAGAT GCGCCACAGG
 101  CAGGTTCTCA AGGACAGGGC GCGCCATCCA CACAAGGCAG CCAAGATATG
 151  GCGGCAGTTT CGGCAGAAAA TACAGGCAAT GGCGGTGCGG CAACAACGGA
 201  CAAACCCAAA AATGAAGACG AGGGACCGCA AAATGATATG CCGCAAAATT
 251  CCGCCGAATC CGCAAATCAA ACAGGGAACA ACCAACCCGC CGATTCTTCA
 301  GATTCCGCCC CCGCGTCAAA CCCTGCACCT GCGAATGGCG GTAGCAATTT
 351  TGGAAGGGTT GATTTGGCTA ATGGCGTTTT GATTGATGGG CCGTCGCAAA
 401  ATATAACGTT GACCCACTGT AAAGGCGATT CTTGTAATGG TGATAATTTA
 451  TTGGATGAAG AAGCACCGTC AAAATCAGAA TTTGAAAATT TAAATGAGTC
 501  TGAACGAATT GAGAAATATA AGAAAGATGG GAAAAGCGAT AAATTTACTA
 551  ATTTGGTTGC GACAGCAGTT CAAGCTAATG GAACTAACAA ATATGTCATC
 601  ATTTATAAAG ACAAGTCCGC TTCATCTTCA TCTGCGCGAT TCAGGCGTTC
 651  TGCACGGTCG AGGAGGTCGC TTCCTGCCGA GATGCCGCTA ATCCCCGTCA
 701  ATCAGGCGGA TACGCTGATT GTCGATGGGG AAGCGGTCAG CCTGACGGGG
 751  CATTCCGGCA ATATCTTCGC GCCCGAAGGG AATTACCGGT ATCTGACTTA
 801  CGGGGCGGAA AAATTGCCCG GCGGATCGTA TGCCCTCCGT GTGCAAGGCG
 851  AACCGGCAAA AGGCGAAATG CTTGCTGGCA CGGCCGTGTA CAACGGCGAA
 901  GTGCTGCATT TTCATACGGA AAACGGCCGT CCGTACCCGA CTAGAGGCAG
 951  GTTTGCCGCA AAAGTCGATT TCGGCAGCAA ATCTGTGGAC GGCATTATCG
1001  ACAGCGGCGA TGATTTGCAT ATGGGTACGC AAAAATTCAA AGCCGCCATC
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1051  GATGGAAACG GCTTTAAGGG GACTTGGACG GAAAATGGCG GCGGGGATGT
1101  TTCCGGAAGG TTTTACGGCC CGGCCGGCGA GGAAGTGGCG GGAAAATACA
1151  GCTATCGCCC GACAGATGCG GAAAAGGGCG GATTCGGCGT GTTTGCCGGC
1201  AAAAAAGAGC AGGATGGATC CGGAGGAGGA GGATGCCAAA GCAAGAGCAT
1251  CCAAACCTTT CCGCAACCCG ACACATCCGT CATCAACGGC CCGGACCGGC
1301  CGGTCGGCAT CCCCGACCCC GCCGGAACGA CGGTCGGCGG CGGCGGGGCC
1351  GTCTATACCG TTGTACCGCA CCTGTCCCTG CCCCACTGGG CGGCGCAGGA
1401  TTTCGCCAAA AGCCTGCAAT CCTTCCGCCT CGGCTGCGCC AATTTGAAAA
1451  ACCGCCAAGG CTGGCAGGAT GTGTGCGCCC AAGCCTTTCA AACCCCCGTC
1501  CATTCCTTTC AGGCAAAACA GTTTTTTGAA CGCTATTTCA CGCCGTGGCA
1551  GGTTGCAGGC AACGGAAGCC TTGCCGGTAC GGTTACCGGC TATTACGAGC
1601  CGGTGCTGAA GGGCGACGAC AGGCGGACGG CACAAGCCCG CTTCCCGATT
1651  TACGGTATTC CCGACGATTT TATCTCCGTC CCCCTGCCTG CCGGTTTGCG
1701  GAGCGGAAAA GCCCTTGTCC GCATCAGGCA GACGGGAAAA AACAGCGGCA
1751  CAATCGACAA TACCGGCGGC ACACATACCG CCGACCTCTC CCGATTCCCC
1801  ATCACCGCGC GCACAACGGC AATCAAAGGC AGGTTTGAAG GAAGCCGCTT
1851  CCTCCCCTAC CACACGCGCA ACCAAATCAA CGGCGGCGCG CTTGACGGCA
1901  AAGCCCCGAT ACTCGGTTAC GCCGAAGACC CCGTCGAACT TTTTTTTATG
1951  CACATCCAAG GCTCGGGCCG TCTGAAAACC CCGTCCGGCA AATACATCCG
2001  CATCGGCTAT GCCGACAAAA ACGAACATCC CTACGTTTCC ATCGGACGCT
2051  ATATGGCGGA CAAAGGCTAC CTCAAGCTCG GGCAGACCTC GATGCAGGGC
2101  ATCAAAGCCT ATATGCGGCA AAATCCGCAA CGCCTCGCCG AAGTTTTGGG
2151  TCAAAACCCC AGCTATATCT TTTTCCGCGA GCTTGCCGGA AGCAGCAATG
2201  ACGGTCCCGT CGGCGCACTG GGCACGCCGT TGATGGGGGA ATATGCCGGC
2251  GCAGTCGACC GGCACTACAT TACCTTGGGC GCGCCCTTAT TTGTCGCCAC
2301  CGCCCATCCG GTTACCCGCA AAGCCCTCAA CCGCCTGATT ATGGCGCAGG
2351  ATACCGGCAG CGCGATTAAA GGCGCGGTGC GCGTGGATTA TTTTTGGGGA
2401  TACGGCGACG AAGCCGGCGA ACTTGCCGGC AAACAGAAAA CCACGGGTTA
2451  CGTCTGGCAG CTCCTACCCA ACGGTATGAA GCCCGAATAC CGCCCGTAAC
2501  TCGAG
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   1  MASPDVKSAD TLSKPAAPVV AEKETEVKED APQAGSQGQG APSTQGSQDM
  51  AAVSAENTGN GGAATTDKPK NEDEGPQNDM PQNSAESANQ TGNNQPADSS
 101  DSAPASNPAP ANGGSNFGRV DLANGVLIDG PSQNITLTHC KGDSCNGDNL
 151  LDEEAPSKSE FENLNESERI EKYKKDGKSD KFTNLVATAV QANGTNKYVI
 201  IYKDKSASSS SARFRRSARS RRSLPAEMPL IPVNQADTLI VDGEAVSLTG
 251  HSGNIFAPEG NYRYLTYGAE KLPGGSYALR VQGEPAKGEM LAGTAVYNGE
 301  VLHFHTENGR PYPTRGRFAA KVDFGSKSVD GIIDSGDDLH MGTQKFKAAI
 351  DGNGFKGTWT ENGGGDVSGR FYGPAGEEVA GKYSYRPTDA EKGGFGVFAG
 401  KKEQDGSGGG GCQSKSIQTF PQPDTSVING PDRPVGIPDP AGTTVGGGGA
 451  VYTVVPHLSL PHWAAQDFAK SLQSFRLGCA NLKNRQGWQD VCAQAFQTPV
 501  HSFQAKQFFE RYFTPWQVAG NGSLAGTVTG YYEPVLKGDD RRTAQARFPI
 551  YGIPDDFISV PLPAGLRSGK ALVRIRQTGK NSGTIDNTGG THTADLSRFP
 601  ITARTTAIKG RFEGSRFLPY HTRNQINGGA LDGKAPILGY AEDPVELFFM
 651  HIQGSGRLKT PSGKYIRIGY ADKNEHPYVS IGRYMADKGY LKLGQTSMQG
 701  IKAYMRQNPQ RLAEVLGQNP SYIFFRELAG SSNDGPVGAL GTPLMGEYAG
 751  AVDRHYITLG APLFVATAHP VTRKALNRLI MAQDTGSAIK GAVRVDYFWG
 801  YGDEAGELAG KQKTTGYVWQ LLPNGMKPEY RP*
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ΔG287–953

```
   1 ATGGCTAGCC CCGATGTTAA ATCGGCGGAC ACGCTGTCAA AACCGGCCGC
  51 TCCTGTTGTT GCTGAAAAAG AGACAGAGGT AAAAGAAGAT GCGCCACAGG
 101 CAGGTTCTCA AGGACAGGGC GCGCCATCCA CACAAGGCAG CCAAGATATG
 151 GCGGCAGTTT CGGCAGAAAA TACAGGCAAT GGCGGTGCGG CAACAACGGA
 201 CAAACCCAAA AATGAAGACG AGGGACCGCA AAATGATATG CCGCAAAATT
 251 CCGCCGAATC CGCAAATCAA ACAGGGAACA ACCAACCCGC CGATTCTTCA
 301 GATTCCGCCC CCGCGTCAAA CCCTGCACCT GCGAATGGCG GTAGCAATTT
 351 TGGAAGGGTT GATTTGGCTA ATGGCGTTTT GATTGATGGG CCGTCGCAAA
 401 ATATAACGTT GACCCACTGT AAAGGCGATT CTTGTAATGG TGATAATTTA
 451 TTGGATGAAG AAGCACCGTC AAAATCAGAA TTTGAAAATT TAAATGAGTC
 501 TGAACGAATT GAGAAATATA AGAAAGATGG GAAAAGCGAT AAATTTACTA
 551 ATTTGGTTGC GACAGCAGTT CAAGCTAATG GAACTAACAA ATATGTCATC
 601 ATTTATAAAG ACAAGTCCGC TTCATCTTCA TCTGCGCGAT TCAGGCGTTC
 651 TGCACGGTCG AGGAGGTCGC TTCCTGCCGA GATGCCGCTA ATCCCCGTCA
 701 ATCAGGCGGA TACGCTGATT GTCGATGGGG AAGCGGTCAG CCTGACGGGG
 751 CATTCCGGCA ATATCTTCGC GCCCGAAGGG AATTACCGGT ATCTGACTTA

 801 CGGGGCGGAA AAATTGCCCG GCGGATCGTA TGCCCTCCGT GTGCAAGGCG
 851 AACCGGCAAA AGGCGAAATG CTTGCTGGCA CGGCCGTGTA CAACGGCGAA
 901 GTGCTGCATT TTCATACGGA AAACGGCCGT CCGTACCCGA CTAGAGGCAG
 951 GTTTGCCGCA AAAGTCGATT TCGGCAGCAA ATCTGTGGAC GGCATTATCG
1001 ACAGCGGCGA TGATTTGCAT ATGGGTACGC AAAAATTCAA AGCCGCCATC
1051 GATGGAAACG GCTTTAAGGG GACTTGGACG GAAAATGGCG GCGGGGATGT
1101 TTCCGGAAGG TTTTACGGCC CGGCCGGCGA GGAAGTGGCG GGAAAATACA
1151 GCTATCGCCC GACAGATGCG GAAAAGGGCG GATTCGGCGT GTTTGCCGGC
1201 AAAAAAGAGC AGGATGGATC CGGAGGAGGA GGAGCCACCT ACAAAGTGGA
1251 CGAATATCAC GCCAACGCCC GTTTCGCCAT CGACCATTTC AACACCAGCA
1301 CCAACGTCGG CGGTTTTTAC GGTCTGACCG GTTCCGTCGA GTTCGACCAA
1351 GCAAAACGCG ACGGTAAAAT CGACATCACC ATCCCCGTTG CCAACCTGCA
1401 AAGCGGTTCG CAACACTTTA CCGACCACCT GAAATCAGCC GACATCTTCG
1451 ATGCCGCCCA ATATCCGGAC ATCCGCTTTG TTTCCACCAA ATTCAACTTC
1501 AACGGCAAAA AACTGGTTTC CGTTGACGGC AACCTGACCA TGCACGGCAA
1551 AACCGCCCCC GTCAAACTCA AAGCCGAAAA ATTCAACTGC TACCAAAGCC
1601 CGATGGCGAA AACCGAAGTT TGCGGCGGCG ACTTCAGCAC CACCATCGAC
1651 CGCACCAAAT GGGGCGTGGA CTACCTCGTT AACGTTGGTA TGACCAAAAG
1701 CGTCCGCATC GACATCCAAA TCGAGGCAGC CAAACAATAA CTCGAG
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   1 MASPDVKSAD TLSKPAAPVV AEKETEVKED APQAGSQGQG APSTQGSQDM
  51 AAVSAENTGN GGAATTDKPK NEDEGPQNDM PQNSAESANQ TGNNQPADSS
 101 DSAPASNPAP ANGGSNFGRV DLANGVLIDG PSQNITLTHC KGDSCNGDNL
 151 LDEEAPSKSE FENLNESERI EKYKKDGKSD KFTNLVATAV QANGTNKYVI
 201 IYKDKSASSS SARFRRSARS RRSLPAEMPL IPVNQADTLI VDGEAVSLTG
 251 HSGNIFAPEG NYRYLTYGAE KLPGGSYALR VQGEPAKGEM LAGTAVYNGE
 301 VLHFHTENGR PYPTRGRFAA KVDFGSKSVD GIIDSGDDLH MGTQKFKAAI
 351 DGNGFKGTWT ENGGGDVSGR FYGPAGEEVA GKYSYRPTDA EKGGFGVFAG
 401 KKEQDGSGGG GATYKVDEYH ANARFAIDHF NTSTNVGGFY GLTGSVEFDQ
 451 AKRDGKIDIT IPVANLQSGS QHFTDHLKSA DIFDAAQYPD IRFVSTKFNF
 501 NGKKLVSVDG NLTMHGKTAP VKLKAEKFNC YQSPMAKTEV CGGDFSTTID
 551 RTKWGVDYLV NVGMTKSVRI DIQIEAAKQ*
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ΔG287–961

```
   1  ATGGCTAGCC CCGATGTTAA ATCGGCGGAC ACGCTGTCAA AACCGGCCGC
  51  TCCTGTTGTT GCTGAAAAAG AGACAGAGGT AAAAGAAGAT GCGCCACAGG
 101  CAGGTTCTCA AGGACAGGGC GCGCCATCCA CACAAGGCAG CCAAGATATG
 151  GCGGCAGTTT CGGCAGAAAA TACAGGCAAT GGCGGTGCGG CAACAACGGA
 201  CAAACCCAAA AATGAAGACG AGGGACCGCA AAATGATATG CCGCAAAATT
 251  CCGCCGAATC CGCAAATCAA ACAGGGAACA ACCAACCCGC CGATTCTTCA
 301  GATTCCGCCC CCGCGTCAAA CCCTGCACCT GCGAATGGCG GTAGCAATTT
 351  TGGAAGGGTT GATTTGGCTA ATGGCGTTTT GATTGATGGG CCGTCGCAAA
 401  ATATAACGTT GACCCACTGT AAAGGCGATT CTTGTAATGG TGATAATTTA
 451  TTGGATGAAG AAGCACCGTC AAAATCAGAA TTTGAAAATT TAAATGAGTC
 501  TGAACGAATT GAGAAATATA AGAAAGATGG GAAAAGCGAT AAATTTACTA
 551  ATTTGGTTGC GACAGCAGTT CAAGCTAATG GAACTAACAA ATATGTCATC
 601  ATTTATAAAG ACAAGTCCGC TTCATCTTCA TCTGCGCGAT TCAGGCGTTC
 651  TGCACGGTCG AGGAGGTCGC TTCCTGCCGA GATGCCGCTA ATCCCCGTCA
 701  ATCAGGCGGA TACGCTGATT GTCGATGGGG AAGCGGTCAG CCTGACGGGG
 751  CATTCCGGCA ATATCTTCGC GCCCGAAGGG AATTACCGGT ATCTGACTTA
 801  CGGGGCGGAA AAATTGCCCG GCGGATCGTA TGCCCTCCGT GTGCAAGGCG
 851  AACCGGCAAA AGGCGAAATG CTTGCTGGCA CGGCCGTGTA CAACGGCGAA
 901  GTGCTGCATT TTCATACGGA AAACGGCCGT CCGTACCCGA CTAGAGGCAG
 951  GTTTGCCGCA AAAGTCGATT TCGGCAGCAA ATCTGTGGAC GGCATTATCG
1001  ACAGCGGCGA TGATTTGCAT ATGGGTACGC AAAAATTCAA AGCCGCCATC
1051  GATGGAAACG GCTTTAAGGG GACTTGGACG GAAAATGGCG GCGGGGATGT
1101  TTCCGGAAGG TTTTACGGCC CGGCCGGCGA GGAAGTGGCG GGAAAATACA
1151  GCTATCGCCC GACAGATGCG GAAAAGGGCG GATTCGGCGT GTTTGCCGGC
1201  AAAAAAGAGC AGGATGGATC CGGAGGAGGA GGAGCCACAA ACGACGACGA
1251  TGTTAAAAAA GCTGCCACTG TGGCCATTGC TGCTGCCTAC AACAATGGCC
1301  AAGAAATCAA CGGTTTCAAA GCTGGAGAGA CCATCTACGA CATTGATGAA
1351  GACGGCACAA TTACCAAAAA AGACGCAACT GCAGCCGATG TTGAAGCCGA
1401  CGACTTTAAA GGTCTGGGTC TGAAAAAAGT CGTGACTAAC CTGACCAAAA
1451  CCGTCAATGA AAACAAACAA AACGTCGATG CCAAAGTAAA AGCTGCAGAA
1501  TCTGAAATAG AAAAGTTAAC AACCAAGTTA GCAGACACTG ATGCCGCTTT
1551  AGCAGATACT GATGCCGCTC TGGATGCAAC CACCAACGCC TTGAATAAAT
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1601  TGGGAGAAAA TATAACGACA TTTGCTGAAG AGACTAAGAC AAATATCGTA
1651  AAAATTGATG AAAAATTAGA AGCCGTGGCT GATACCGTCG ACAAGCATGC
1701  CGAAGCATTC AACGATATCG CCGATTCATT GGATGAAACC AACACTAAGG
1751  CAGACGAAGC CGTCAAAACC GCCAATGAAG CCAAACAGAC GGCCGAAGAA
1801  ACCAAACAAA ACGTCGATGC CAAAGTAAAA GCTGCAGAAA CTGCAGCAGG
1851  CAAAGCCGAA GCTGCCGCTG GCACAGCTAA TACTGCAGCC GACAAGGCCG
1901  AAGCTGTCGC TGCAAAAGTT ACCGACATCA AAGCTGATAT CGCTACGAAC
1951  AAAGATAATA TTGCTAAAAA AGCAAACAGT GCCGACGTGT ACACCAGAGA
2001  AGAGTCTGAC AGCAAATTTG TCAGAATTGA TGGTCTGAAC GCTACTACCG
2051  AAAAATTGGA CACACGCTTG GCTTCTGCTG AAAAATCCAT TGCCGATCAC
2101  GATACTCGCC TGAACGGTTT GGATAAAACA GTGTCAGACC TGCGCAAAGA
2151  AACCCGCCAA GGCCTTGCAG AACAAGCCGC GCTCTCCGGT CTGTTCCAAC
2201  CTTACAACGT GGGTCGGTTC AATGTAACGG CTGCAGTCGG CGGCTACAAA
2251  TCCGAATCGG CAGTCGCCAT CGGTACCGGC TTCCGCTTTA CCGAAAACTT
2301  TGCCGCCAAA GCAGGCGTGG CAGTCGGCAC TTCGTCCGGT TCTTCCGCAG
2351  CCTACCATGT CGGCGTCAAT TACGAGTGGT AACTCGAG
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  1 MASPDVKSAD TLSKPAAPVV AEKETEVKED APQAGSQGQG APSTQGSQDM
 51 AAVSAENTGN GGAATTDKPK NEDEGPQNDM PQNSAESANQ TGNNQPADSS
101 DSAPASNPAP ANGGSNFGRV DLANGVLIDG PSQNITLTHC KGDSCNGDNL
151 LDEEAPSKSE FENLNESERI EKYKKDGKSD KFTNLVATAV QANGTNKYVI
201 IYKDKSASSS SARFRRSARS RRSLPAEMPL IPVNQADTLI VDGEAVSLTG
251 HSGNIFAPEG NYRYLTYGAE KLPGGSYALR VQGEPAKGEM LAGTAVYNGE
301 VLHFHTENGR PYPTRGRFAA KVDFGSKSVD GIIDSGDDLH MGTQKFKAAI
351 DGNGFKGTWT ENGGGDVSGR FYGPAGEEVA GKYSYRPTDA EKGGFGVFAG
401 KKEQDGSGGG GATNDDDVKK AATVAIAAAY NNGQEINGFK AGETIYDIDE
451 DGTITKKDAT AADVEADDFK GLGLKKVVTN LTKTVNENKQ NVDAKVKAAE
501 SEIEKLTTKL ADTDAALADT DAALDATTNA LNKLGENITT FAEETKTNIV
551 KIDEKLEAVA DTVDKHAEAF NDIADSLDET NTKADEAVKT ANEAKQTAEE
601 TKQNVDAKVK AAETAAGKAE AAAGTANTAA DKAEAVAAKV TDIKADIATN
651 KDNIAKKANS ADVYTREESD SKFVRIDGLN ATTEKLDTRL ASAEKSIADH
701 DTRLNGLDKT VSDLRKETRQ GLAEQAALSG LFQPYNVGRF NVTAAVGGYK
751 SESAVAIGTG FRFTENFAAK AGVAVGTSSG SSAAYHVGVN YEW*
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	ELISA	**Bactericidal**
ΔG287-953-His	3834	65536
ΔG287-961-His	108627	65536

[0219] The bactericidal efficacy (homologous strain) of antibodies raised against the hybrid proteins was compared with antibodies raised against simple mixtures of the component antigens (using 287-GST) for 919 and ORF46.1:

	Mixture with 287	**Hybrid with ΔG287**
919	32000	128000
ORF46.1	128	16000

[0220] Data for bactericidal activity against heterologous MenB strains and against serotypes A and C were also obtained:

	919		**ORF46.1**	
Strain	*Mixture*	*Hybrid*	*Mixture*	*Hybrid*
NGH38	1024	32000	-	16384
MC58	512	8192	-	512
BZ232	512	512	-	-
MenA (F6124)	512	32000	-	8192
MenC (C11)	>2048	>2048	-	-
MenC (BZ133)	>4096	64000	-	8192

[0221] The hybrid proteins with ΔG287 at the N-terminus are therefore immunologically superior to simple mixtures, with ΔG287-ORF46.1 being particularly effective, even against heterologous strains. ΔG287-ORF46.1K may be expressed in pET-24b.

[0222] The same hybrid proteins were made using New Zealand strain 394/98 rather than 2996:

ΔG287NZ-919

```
   1  ATGGCTAGCC CCGATGTCAA GTCGGCGGAC ACGCTGTCAA AACCTGCCGC
  51  CCCTGTTGTT TCTGAAAAAG AGACAGAGGC AAAGGAAGAT GCGCCACAGG
 101  CAGGTTCTCA AGGACAGGGC GCGCCATCCG CACAAGGCGG TCAAGATATG
 151  GCGGCGGTTT CGGAAGAAAA TACAGGCAAT GGCGGTGCGG CAGCAACGGA
 201  CAAACCCAAA AATGAAGACG AGGGGGCGCA AAATGATATG CCGCAAAATG
 251  CCGCCGATAC AGATAGTTTG ACACCGAATC ACACCCCGGC TTCGAATATG
 301  CCGGCCGGAA ATATGGAAAA CCAAGCACCG GATGCCGGGG AATCGGAGCA
 351  GCCGGCAAAC CAACCGGATA TGGCAAATAC GGCGGACGGA ATGCAGGGTG
 401  ACGATCCGTC GGCAGGCGGG GAAAATGCCG GCAATACGGC TGCCCAAGGT
 451  ACAAATCAAG CCGAAAACAA TCAAACCGCC GGTTCTCAAA ATCCTGCCTC
 501  TTCAACCAAT CCTAGCGCCA CGAATAGCGG TGGTGATTTT GGAAGGACGA
 551  ACGTGGGCAA TTCTGTTGTG ATTGACGGGC CGTCGCAAAA TATAACGTTG
 601  ACCCACTGTA AAGGCGATTC TTGTAGTGGC AATAATTTCT TGGATGAAGA
 651  AGTACAGCTA AAATCAGAAT TTGAAAAATT AAGTGATGCA GACAAAATAA
 701  GTAATTACAA GAAAGATGGG AAGAATGACG GGAAGAATGA TAAATTTGTC
 751  GGTTTGGTTG CCGATAGTGT GCAGATGAAG GGAATCAATC AATATATTAT
 801  CTTTTATAAA CCTAAACCCA CTTCATTTGC GCGATTTAGG CGTTCTGCAC
 851  GGTCGAGGCG GTCGCTTCCG GCCGAGATGC CGCTGATTCC CGTCAATCAG
 901  GCGGATACGC TGATTGTCGA TGGGGAAGCG GTCAGCCTGA CGGGGCATTC
 951  CGGCAATATC TTCGCGCCCG AAGGGAATTA CCGGTATCTG ACTTACGGGG
1001  CGGAAAAATT GCCCGGCGGA TCGTATGCCC TCCGTGTTCA AGGCGAACCT
1051  TCAAAAGGCG AAATGCTCGC GGGCACGGCA GTGTACAACG GCGAAGTGCT
1101  GCATTTTCAT ACGGAAAACG GCCGTCCGTC CCCGTCCAGA GGCAGGTTTG
1151  CCGCAAAAGT CGATTTCGGC AGCAAATCTG TGGACGGCAT TATCGACAGC
1201  GGCGATGGTT TGCATATGGG TACGCAAAAA TTCAAAGCCG CCATCGATGG
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1301  GAAAGTTTTA CGGCCCGGCC GGCGAGGAAG TGGCGGGAAA ATACAGCTAT
1351  CGCCCAACAG ATGCGGAAAA GGGCGGATTC GGCGTGTTTG CCGGCAAAAA
1401  AGAGCAGGAT GGATCCGGAG GAGGAGGATG CCAAAGCAAG AGCATCCAAA
1451  CCTTTCCGCA ACCCGACACA TCCGTCATCA ACGGCCCGGA CCGGCCGGTC
1501  GGCATCCCCG ACCCCGCCGG AACGACGGTC GGCGGCGGCG GGGCCGTCTA
1551  TACCGTTGTA CCGCACCTGT CCCTGCCCCA CTGGGCGGCG CAGGATTTCG
1601  CCAAAAGCCT GCAATCCTTC CGCCTCGGCT GCGCCAATTT GAAAAACCGC
1651  CAAGGCTGGC AGGATGTGTG CGCCCAAGCC TTTCAAACCC CCGTCCATTC
1701  CTTTCAGGCA AAACAGTTTT TTGAACGCTA TTTCACGCCG TGGCAGGTTG
1751  CAGGCAACGG AAGCCTTGCC GGTACGGTTA CCGGCTATTA CGAGCCGGTG
1801  CTGAAGGGCG ACGACAGGCG GACGGCACAA GCCCGCTTCC CGATTTACGG
1851  TATTCCCGAC GATTTTATCT CCGTCCCCCT GCCTGCCGGT TTGCGGAGCG
1901  GAAAAGCCCT TGTCCGCATC AGGCAGACGG GAAAAAACAG CGGCACAATC
1951  GACAATACCG GCGGCACACA TACCGCCGAC CTCTCCCGAT TCCCCATCAC
2001  CGCGCGCACA ACGGCAATCA AAGGCAGGTT TGAAGGAAGC CGCTTCCTCC

2051  CCTACCACAC GCGCAACCAA ATCAACGGCG GCGCGCTTGA CGGCAAAGCC
2101  CCGATACTCG GTTACGCCGA AGACCCCGTC GAACTTTTTT TTATGCACAT
2151  CCAAGGCTCG GGCCGTCTGA AAACCCCGTC CGGCAAATAC ATCCGCATCG
2201  GCTATGCCGA CAAAAACGAA CATCCCTACG TTTCCATCGG ACGCTATATG
2251  GCGGACAAAG GCTACCTCAA GCTCGGGCAG ACCTCGATGC AGGGCATCAA
2301  AGCCTATATG CGGCAAAATC CGCAACGCCT CGCCGAAGTT TTGGGTCAAA
2351  ACCCCAGCTA TATCTTTTTC CGCGAGCTTG CCGGAAGCAG CAATGACGGT
2401  CCCGTCGGCG CACTGGGCAC GCCGTTGATG GGGGAATATG CCGGCGCAGT
2451  CGACCGGCAC TACATTACCT TGGGCGCGCC CTTATTTGTC GCCACCGCCC
2501  ATCCGGTTAC CCGCAAAGCC CTCAACCGCC TGATTATGGC GCAGGATACC
2551  GGCAGCGCGA TTAAAGGCGC GGTGCGCGTG GATTATTTTT GGGGATACGG
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2651  GGCAGCTCCT ACCCAACGGT ATGAAGCCCG AATACCGCCC GTAAAAGCTT
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101	PAGNMENQAP DAGESEQPAN QPDMANTADG MQGDDPSAGG ENAGNTAAQG
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201	THCKGDSCSG NNFLDEEVQL KSEFEKLSDA DKISNYKKDG KNDGKNDKFV
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301	ADTLIVDGEA VSLTGHSGNI FAPEGNYRYL TYGAEKLPGG SYALRVQGEP
351	SKGEMLAGTA VYNGEVLHFH TENGRPSPSR GRFAAKVDFG SKSVDGIIDS
401	GDGLHMGTQK FKAAIDGNGF KGTWTENGGG DVSGKFYGPA GEEVAGKYSY
451	RPTDAEKGGF GVFAGKKEQD GSGGGGCQSK SIQTFPQPDT SVINGPDRPV
501	GIPDPAGTTV GGGGAVYTVV PHLSLPHWAA QDFAKSLQSF RLGCANLKNR
551	QGWQDVCAQA FQTPVHSFQA KQFFERYFTP WQVAGNGSLA GTVTGYYEPV
601	LKGDDRRTAQ ARFPIYGIPD DFISVPLPAG LRSGKALVRI RQTGKNSGTI
651	DNTGGTHTAD LSRFPITART TAIKGRFEGS RFLPYHTRNQ INGGALDGKA
701	PILGYAEDPV ELFFMHIQGS GRLKTPSGKY IRIGYADKNE HPYVSIGRYM
751	ADKGYLKLGQ TSMQGIKAYM RQNPQRLAEV LGQNPSYIFF RELAGSSNDG
801	PVGALGTPLM GEYAGAVDRH YITLGAPLFV ATAHPVTRKA LNRLIMAQDT
851	GSAIKGAVRV DYFWGYGDEA GELAGKQKTT GYVWQLLPNG MKPEYRP*

ΔG287NZ-953

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151	GCGGCGGTTT CGGAAGAAAA TACAGGCAAT GGCGGTGCGG CAGCAACGGA
201	CAAACCCAAA AATGAAGACG AGGGGGCGCA AAATGATATG CCGCAAAATG
251	CCGCCGATAC AGATAGTTTG ACACCGAATC ACACCCCGGC TTCGAATATG
301	CCGGCCGGAA ATATGGAAAA CCAAGCACCG GATGCCGGGG AATCGGAGCA
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701	GTAATTACAA GAAAGATGGG AAGAATGACG GGAAGAATGA TAAATTTGTC
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851	GGTCGAGGCG GTCGCTTCCG GCCGAGATGC CGCTGATTCC CGTCAATCAG
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1251	AAACGGCTTT AAGGGGACTT GGACGGAAAA TGGCGGCGGG GATGTTTCCG
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1651  GCCCAATATC CGGACATCCG CTTTGTTTCC ACCAAATTCA ACTTCAACGG
1701  CAAAAAACTG GTTTCCGTTG ACGGCAACCT GACCATGCAC GGCAAAACCG
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501  VGGFYGLTGS VEFDQAKRDG KIDITIPVAN LQSGSQHFTD HLKSADIFDA
551  AQYPDIRFVS TKFNFNGKKL VSVDGNLTMH GKTAPVKLKA EKFNCYQSPM
601  AKTEVCGGDF STTIDRTKWG VDYLVNVGMT KSVRIDIQIE AAKQ*
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ΔG287NZ-961

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2001  ACAAAACGTC GATGCCAAAG TAAAAGCTGC AGAAACTGCA GCAGGCAAAG
2051  CCGAAGCTGC CGCTGGCACA GCTAATACTG CAGCCGACAA GGCCGAAGCT
2101  GTCGCTGCAA AAGTTACCGA CATCAAAGCT GATATCGCTA CGAACAAAGA

2151  TAATATTGCT AAAAAAGCAA ACAGTGCCGA CGTGTACACC AGAGAAGAGT
2201  CTGACAGCAA ATTTGTCAGA ATTGATGGTC TGAACGCTAC TACCGAAAAA
2251  TTGGACACAC GCTTGGCTTC TGCTGAAAAA TCCATTGCCG ATCACGATAC
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2351  GCCAAGGCCT TGCAGAACAA GCCGCGCTCT CCGGTCTGTT CCAACCTTAC
2401  AACGTGGGTC GGTTCAATGT AACGGCTGCA GTCGGCGGCT ACAAATCCGA
2451  ATCGGCAGTC GCCATCGGTA CCGGCTTCCG CTTTACCGAA AACTTTGCCG
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2551  CATGTCGGCG TCAATTACGA GTGGTAAAAG CTT
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201   THCKGDSCSG NNFLDEEVQL KSEFEKLSDA DKISNYKKDG KNDGKNDKFV
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301   ADTLIVDGEA VSLTGHSGNI FAPEGNYRYL TYGAEKLPGG SYALRVQGEP
351   SKGEMLAGTA VYNGEVLHFH TENGRPSPSR GRFAAKVDFG SKSVDGIIDS
401   GDGLHMGTQK FKAAIDGNGF KGTWTENGGG DVSGKFYGPA GEEVAGKYSY
451   RPTDAEKGGF GVFAGKKEQD GSGGGGATND DDVKKAATVA IAAAYNNGQE
501   INGFKAGETI YDIDEDGTIT KKDATAADVE ADDFKGLGLK KVVTNLTKTV
551   NENKQNVDAK VKAAESEIEK LTTKLADTDA ALADTDAALD ATTNALNKLG
601   ENITTFAEET KTNIVKIDEK LEAVADTVDK HAEAFNDIAD SLDETNTKAD
651   EAVKTANEAK QTAEETKQNV DAKVKAAETA AGKAEAAAGT ANTAADKAEA
701   VAAKVTDIKA DIATNKDNIA KKANSADVYT REESDSKFVR IDGLNATTEK
751   LDTRLASAEK SIADHDTRLN GLDKTVSDLR KETRQGLAEQ AALSGLFQPY
801   NVGRFNVTAA VGGYKSESAV AIGTGFRFTE NFAAKAGVAV GTSSGSSAAY
851   HVGVNYEW*
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ΔG983 and hybrids

[0223] Bactericidal titres generated in response to ΔG983 (His-fusion) were measured against various strains, including the homologous 2996 strain:

	2996	NGH38	BZ133
ΔG983	512	128	128

[0224] ΔG983 was also expressed as a hybrid, with ORF46.1, 741, 961 or 961c at its C-terminus:

ΔG983-ORF46.1

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   1  ATGACTTCTG CGCCCGACTT CAATGCAGGC GGTACCGGTA TCGGCAGCAA
  51  CAGCAGAGCA ACAACAGCGA AATCAGCAGC AGTATCTTAC GCCGGTATCA
 101  AGAACGAAAT GTGCAAAGAC AGAAGCATGC TCTGTGCCGG TCGGGATGAC
 151  GTTGCGGTTA CAGACAGGGA TGCCAAAATC AATGCCCCCC CCCCGAATCT
 201  GCATACCGGA GACTTTCCAA ACCCAAATGA CGCATACAAG AATTTGATCA
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 451  GCTTCTTTCG ACGATGAGGC CGTTATAGAG ACTGAAGCAA AGCCGACGGA
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1001  GCGTAGACCG CAGTGGAGAA AAGTTCAAAC GGGAAATGTA TGGAGAACCG
1051  GGTACAGAAC CGCTTGAGTA TGGCTCCAAC CATTGCGGAA TTACTGCCAT
1101  GTGGTGCCTG TCGGCACCCT ATGAAGCAAG CGTCCGTTTC ACCCGTACAA
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4401  CGAGCACCAC CACCACCACC ACTGA
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 201  ATLHIMNTND ETKNEMMVAA IRNAWVKLGE RGVRIVNNSF GTTSRAGTAD
 251  LFQIANSEEQ YRQALLDYSG GDKTDEGIRL MQQSDYGNLS YHIRNKNMLF
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 351  GTEPLEYGSN HCGITAMWCL SAPYEASVRF TRTNPIQIAG TSFSAPIVTG
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ΔG983-741

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1651	GACCAATCCG GCGCAAACGA AACCGTACAC ATCAAAGGCA GTCTGCAGCT

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 151  ASFDDEAVIE TEAKPTDIRH VKEIGHIDLV SHIIGGRSVD GRPAGGIAPD
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ΔG983-961

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 601   GAGYLNSTGR RVPFLSAAKI GQDYSFFTNI ETDGGLLASL DSVEKTAGSE
 651   GDTLSYYVRR GNAARTASAA AHSAPAGLKH AVEQGGSNLE NLMVELDASE
 701   SSATPETVET AAADRTDMPG IRPYGATFRA AAAVQHANAA DGVRIFNSLA
 751   ATVYADSTAA HADMQGRRLK AVSDGLDHNG TGLRVIAQTQ QDGGTWEQGG
 801   VEGKMRGSTQ TVGIAAKTGE NTTAAATLGM GRSTWSENSA NAKTDSISLF
 851   AGIRHDAGDI GYLKGLFSYG RYKNSISRST GADEHAEGSV NGTLMQLGAL
 901   GGVNVPFAAT GDLTVEGGLR YDLLKQDAFA EKGSALGWSG NSLTEGTLVG
 951   LAGLKLSQPL SDKAVLFATA GVERDLNGRD YTVTGGFTGA TAATGKTGAR
1001   NMPHTRLVAG LGADVEFGNG WNGLARYSYA GSKQYGNHSG RVGVGYRFLE
1051   GGGGTGSATN DDDVKKAATV AIAAAYNNGQ EINGFKAGET IYDIDEDGTI
1101   TKKDATAADV EADDFKGLGL KKVVTNLTKT VNENKQNVDA KVKAAESEIE
1151   KLTTKLADTD AALADTDAAL DATTNALNKL GENITTFAEE TKTNIVKIDE
1201   KLEAVADTVD KHAEAFNDIA DSLDETNTKA DEAVKTANEA KQTAEETKQN
1251   VDAKVKAAET AAGKAEAAAG TANTAADKAE AVAAKVTDIK ADIATNKDNI
1301   AKKANSADVY TREESDSKFV RIDGLNATTE KLDTRLASAE KSIADHDTRL
1351   NGLDKTVSDL RKETRQGLAE QAALSGLFQP YNVGRFNVTA AVGGYKSESA
1401   VAIGTGFRFT ENFAAKAGVA VGTSSGSSAA YHVGVNYEWL EHHHHHH*
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ΔG983-961c

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  1   ATGACTTCTG CGCCCGACTT CAATGCAGGC GGTACCGGTA TCGGCAGCAA
 51   CAGCAGAGCA ACAACAGCGA AATCAGCAGC AGTATCTTAC GCCGGTATCA
101   AGAACGAAAT GTGCAAAGAC AGAAGCATGC TCTGTGCCGG TCGGGATGAC
151   GTTGCGGTTA CAGACAGGGA TGCCAAAATC AATGCCCCCC CCCCGAATCT
201   GCATACCGGA GACTTTCCAA ACCCAAATGA CGCATACAAG AATTTGATCA
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251   ACCTCAAACC TGCAATTGAA GCAGGCTATA CAGGACGCGG GGTAGAGGTA
301   GGTATCGTCG ACACAGGCGA ATCCGTCGGC AGCATATCCT TTCCCGAACT
351   GTATGGCAGA AAAGAACACG GCTATAACGA AAATTACAAA AACTATACGG
401   CGTATATGCG GAAGGAAGCG CCTGAAGACG GAGGCGGTAA AGACATTGAA
451   GCTTCTTTCG ACGATGAGGC CGTTATAGAG ACTGAAGCAA AGCCGACGGA
501   TATCCGCCAC GTAAAAGAAA TCGGACACAT CGATTTGGTC TCCCATATTA
551   TTGGCGGGCG TTCCGTGGAC GGCAGACCTG CAGGCGGTAT TGCGCCCGAT
601   GCGACGCTAC ACATAATGAA TACGAATGAT GAAACCAAGA ACGAAATGAT
651   GGTTGCAGCC ATCCGCAATG CATGGGTCAA GCTGGGCGAA CGTGGCGTGC
701   GCATCGTCAA TAACAGTTTT GGAACAACAT CGAGGGCAGG CACTGCCGAC
751   CTTTTCCAAA TAGCCAATTC GGAGGAGCAG TACCGCCAAG CGTTGCTCGA
801   CTATTCCGGC GGTGATAAAA CAGACGAGGG TATCCGCCTG ATGCAACAGA
851   GCGATTACGG CAACCTGTCC TACCACATCC GTAATAAAAA CATGCTTTTC
901   ATCTTTTCGA CAGGCAATGA CGCACAAGCT CAGCCCAACA CATATGCCCT
951   ATTGCCATTT TATGAAAAAG ACGCTCAAAA AGGCATTATC ACAGTCGCAG
1001  GCGTAGACCG CAGTGGAGAA AAGTTCAAAC GGGAAATGTA TGGAGAACCG
1051  GGTACAGAAC CGCTTGAGTA TGGCTCCAAC CATTGCGGAA TTACTGCCAT
1101  GTGGTGCCTG TCGGCACCCT ATGAAGCAAG CGTCCGTTTC ACCCGTACAA
1151  ACCCGATTCA AATTGCCGGA ACATCCTTTT CCGCACCCAT CGTAACCGGC
1201  ACGGCGGCTC TGCTGCTGCA GAAATACCCG TGGATGAGCA ACGACAACCT
1251  GCGTACCACG TTGCTGACGA CGGCTCAGGA CATCGGTGCA GTCGGCGTGG
1301  ACAGCAAGTT CGGCTGGGGA CTGCTGGATG CGGGTAAGGC CATGAACGGA
1351  CCCGCGTCCT TTCCGTTCGG CGACTTTACC GCCGATACGA AAGGTACATC
1401  CGATATTGCC TACTCCTTCC GTAACGACAT TTCAGGCACG GGCGGCCTGA
1451  TCAAAAAAGG CGGCAGCCAA CTGCAACTGC ACGGCAACAA CACCTATACG
1501  GGCAAAACCA TTATCGAAGG CGGTTCGCTG GTGTTGTACG GCAACAACAA
1551  ATCGGATATG CGCGTCGAAA CCAAAGGTGC GCTGATTTAT AACGGGGCGG
1601  CATCCGGCGG CAGCCTGAAC AGCGACGGCA TTGTCTATCT GGCAGATACC
1651  GACCAATCCG GCGCAAACGA AACCGTACAC ATCAAAGGCA GTCTGCAGCT
1701  GGACGGCAAA GGTACGCTGT ACACACGTTT GGGCAAACTG CTGAAAGTGG
1751  ACGGTACGGC GATTATCGGC GGCAAGCTGT ACATGTCGGC ACGCGGCAAG
1801  GGGGCAGGCT ATCTCAACAG TACCGGACGA CGTGTTCCCT TCCTGAGTGC
1851  CGCCAAAATC GGGCAGGATT ATTCTTTCTT CACAAACATC GAAACCGACG
1901  GCGGCCTGCT GGCTTCCCTC GACAGCGTCG AAAAAACAGC GGGCAGTGAA
1951  GGCGACACGC TGTCCTATTA TGTCCGTCGC GGCAATGCGG CACGGACTGC
2001  TTCGGCAGCG GCACATTCCG CGCCCGCCGG TCTGAAACAC GCCGTAGAAC
2051  AGGGCGGCAG CAATCTGGAA AACCTGATGG TCGAACTGGA TGCCTCCGAA
2101  TCATCCGCAA CACCCGAGAC GGTTGAAACT GCGGCAGCCG ACCGCACAGA
2151  TATGCCGGGC ATCCGCCCCT ACGGCGCAAC TTTCCGCGCA GCGGCAGCCG
2201  TACAGCATGC GAATGCCGCC GACGGTGTAC GCATCTTCAA CAGTCTCGCC
2251  GCTACCGTCT ATGCCGACAG TACCGCCGCC CATGCCGATA TGCAGGGACG
2301  CCGCCTGAAA GCCGTATCGG ACGGGTTGGA CCACAACGGC ACGGGTCTGC
2351  GCGTCATCGC GCAAACCCAA CAGGACGGTG GAACGTGGGA ACAGGGCGGT
2401  GTTGAAGGCA AAATGCGCGG CAGTACCCAA ACCGTCGGCA TTGCCGCGAA
2451  AACCGGCGAA AATACGACAG CAGCCGCCAC ACTGGGCATG GGACGCAGCA
2501  CATGGAGCGA AAACAGTGCA AATGCAAAAA CCGACAGCAT TAGTCTGTTT
2551  GCAGGCATAC GGCACGATGC GGGCGATATC GGCTATCTCA AAGGCCTGTT
2601  CTCCTACGGA CGCTACAAAA ACAGCATCAG CCGCAGCACC GGTGCGGACG
2651  AACATGCGGA AGGCAGCGTC AACGGCACGC TGATGCAGCT GGGCGCACTG
2701  GGCGGTGTCA ACGTTCCGTT TGCCGCAACG GGAGATTTGA CGGTCGAAGG
2751  CGGTCTGCGC TACGACCTGC TCAAACAGGA TGCATTCGCC GAAAAAGGCA
2801  GTGCTTTGGG CTGGAGCGGC AACAGCCTCA CTGAAGGCAC GCTGGTCGGA
2851  CTCGCGGGTC TGAAGCTGTC GCAACCCTTG AGCGATAAAG CCGTCCTGTT
2901  TGCAACGGCG GGCGTGGAAC GCGACCTGAA CGGACGCGAC TACACGGTAA
2951  CGGGCGGCTT TACCGGCGCG ACTGCAGCAA CCGGCAAGAC GGGGGCACGC
3001  AATATGCCGC ACACCCGTCT GGTTGCCGGC CTGGGCGCGG ATGTCGAATT
3051  CGGCAACGGC TGGAACGGCT TGGCACGTTA CAGCTACGCC GGTTCCAAAC
3101  AGTACGGCAA CCACAGCGGA CGAGTCGGCG TAGGCTACCG GTTCCTCGAG
3151  GGTGGCGGAG GCACTGGATC CGCCACAAAC GACGACGATG TTAAAAAAGC
3201  TGCCACTGTG GCCATTGCTG CTGCCTACAA CAATGGCCAA GAAATCAACG
3251  GTTTCAAAGC TGGAGAGACC ATCTACGACA TTGATGAAGA CGGCACAATT
3301  ACCAAAAAAG ACGCAACTGC AGCCGATGTT GAAGCCGACG ACTTTAAAGG
3351  TCTGGGTCTG AAAAAAGTCG TGACTAACCT GACCAAAACC GTCAATGAAA
3401  ACAAACAAAA CGTCGATGCC AAAGTAAAAG CTGCAGAATC TGAAATAGAA
3451  AAGTTAACAA CCAAGTTAGC AGACACTGAT GCCGCTTTAG CAGATACTGA
3501  TGCCGCTCTG GATGCAACCA CCAACGCCTT GAATAAATTG GGAGAAAATA
3551  TAACGACATT TGCTGAAGAG ACTAAGACAA ATATCGTAAA AATTGATGAA
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3601    AAATTAGAAG CCGTGGCTGA TACCGTCGAC AAGCATGCCG AAGCATTCAA
3651    CGATATCGCC GATTCATTGG ATGAAACCAA CACTAAGGCA GACGAAGCCG
3701    TCAAAACCGC CAATGAAGCC AAACAGACGG CCGAAGAAAC CAAACAAAAC
3751    GTCGATGCCA AAGTAAAAGC TGCAGAAACT GCAGCAGGCA AAGCCGAAGC
3801    TGCCGCTGGC ACAGCTAATA CTGCAGCCGA CAAGGCCGAA GCTGTCGCTG
3851    CAAAAGTTAC CGACATCAAA GCTGATATCG CTACGAACAA AGATAATATT
3901    GCTAAAAAAG CAAACAGTGC CGACGTGTAC ACCAGAGAAG AGTCTGACAG
3951    CAAATTTGTC AGAATTGATG GTCTGAACGC TACTACCGAA AAATTGGACA
4001    CACGCTTGGC TTCTGCTGAA AAATCCATTG CCGATCACGA TACTCGCCTG
4051    AACGGTTTGG ATAAAACAGT GTCAGACCTG CGCAAAGAAA CCCGCCAAGG
4101    CCTTGCAGAA CAAGCCGCGC TCTCCGGTCT GTTCCAACCT TACAACGTGG
4151    GTCTCGAGCA CCACCACCAC CACCACTGA
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   1    MTSAPDFNAG GTGIGSNSRA TTAKSAAVSY AGIKNEMCKD RSMLCAGRDD
  51    VAVTDRDAKI NAPPPNLHTG DFPNPNDAYK NLINLKPAIE AGYTGRGVEV
 101    GIVDTGESVG SISFPELYGR KEHGYNENYK NYTAYMRKEA PEDGGGKDIE
 151    ASFDDEAVIE TEAKPTDIRH VKEIGHIDLV SHIIGGRSVD GRPAGGIAPD
 201    ATLHIMNTND ETKNEMMVAA IRNAWVKLGE RGVRIVNNSF GTTSRAGTAD
 251    LFQIANSEEQ YRQALLDYSG GDKTDEGIRL MQQSDYGNLS YHIRNKNMLF
 301    IFSTGNDAQA QPNTYALLPF YEKDAQKGII TVAGVDRSGE KFKREMYGEP
 351    GTEPLEYGSN HCGITAMWCL SAPYEASVRF TRTNPIQIAG TSFSAPIVTG
 401    TAALLLQKYP WMSNDNLRTT LLTTAQDIGA VGVDSKFGWG LLDAGKAMNG
 451    PASFPFGDFT ADTKGTSDIA YSFRNDISGT GGLIKKGGSQ LQLHGNNTYT
 501    GKTIIEGGSL VLYGNNKSDM RVETKGALIY NGAASGGSLN SDGIVYLADT
 551    DQSGANETVH IKGSLQLDGK GTLYTRLGKL LKVDGTAIIG GKLYMSARGK
 601    GAGYLNSTGR RVPFLSAAKI GQDYSFFTNI ETDGGLLASL DSVEKTAGSE
 651    GDTLSYYVRR GNAARTASAA AHSAPAGLKH AVEQGGSNLE NLMVELDASE
 701    SSATPETVET AAADRTDMPG IRPYGATFRA AAAVQHANAA DGVRIFNSLA
 751    ATVYADSTAA HADMQGRRLK AVSDGLDHNG TGLRVIAQTQ QDGGTWEQGG
 801    VEGKMRGSTQ TVGIAAKTGE NTTAAATLGM GRSTWSENSA NAKTDSISLF
 851    AGIRHDAGDI GYLKGLFSYG RYKNSISRST GADEHAEGSV NGTLMQLGAL
 901    GGVNVPFAAT GDLTVEGGLR YDLLKQDAFA EKGSALGWSG NSLTEGTLVG
 951    LAGLKLSQPL SDKAVLFATA GVERDLNGRD YTVTGGFTGA TAATGKTGAR
1001    NMPHTRLVAG LGADVEFGNG WNGLARYSYA GSKQYGNHSG RVGVGYRFLE
1051    GGGGTGSATN DDDVKKAATV AIAAAYNNGQ EINGFKAGET IYDIDEDGTI
1101    TKKDATAADV EADDFKGLGL KKVVTNLTKT VNENKQNVDA KVKAAESEIE
1151    KLTTKLADTD AALADTDAAL DATTNALNKL GENITTFAEE TKTNIVKIDE
1201    KLEAVADTVD KHAEAFNDIA DSLDETNTKA DEAVKTANEA KQTAEETKQN
1251    VDAKVKAAET AAGKAEAAAG TANTAADKAE AVAAKVTDIK ADIATNKDNI
1301    AKKANSADVY TREESDSKFV RIDGLNATTE KLDTRLASAE KSIADHDTRL
1351    NGLDKTVSDL RKETRQGLAE QAALSGLFQP YNVGLEHHHH HH*
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ΔG741 and hybrids

[0225] Bactericidal titres generated in response to ΔG741 (His-fusion) were measured against various strains, including the homologous 2996 strain:

	2996	MC58	NGH38	F6124	BZ133
ΔG741	512	131072	>2048	16384	>2048

[0226] As can be seen, the ΔG741-induced anti-bactericidal titre is particularly high against heterologous strain MC58.

[0227] ΔG741 was also fused directly in-frame upstream of proteins 961, 961c, 983 and ORF46.1:

ΔG741-961

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   1  ATGGTCGCCG CCGACATCGG TGCGGGGCTT GCCGATGCAC TAACCGCACC
  51  GCTCGACCAT AAAGACAAAG GTTTGCAGTC TTTGACGCTG GATCAGTCCG
 101  TCAGGAAAAA CGAGAAACTG AAGCTGGCGG CACAAGGTGC GGAAAAAACT
 151  TATGGAAACG GTGACAGCCT CAATACGGGC AAATTGAAGA ACGACAAGGT
 201  CAGCCGTTTC GACTTTATCC GCCAAATCGA AGTGGACGGG CAGCTCATTA

 251  CCTTGGAGAG TGGAGAGTTC CAAGTATACA AACAAAGCCA TTCCGCCTTA
 301  ACCGCCTTTC AGACCGAGCA AATACAAGAT TCGGAGCATT CCGGGAAGAT
 351  GGTTGCGAAA CGCCAGTTCA GAATCGGCGA CATAGCGGGC GAACATACAT
 401  CTTTTGACAA GCTTCCCGAA GGCGGCAGGG CGACATATCG CGGGACGGCG
 451  TTCGGTTCAG ACGATGCCGG CGGAAAACTG ACCTACACCA TAGATTTCGC
 501  CGCCAAGCAG GGAAACGGCA AAATCGAACA TTTGAAATCG CCAGAACTCA
 551  ATGTCGACCT GGCCGCCGCC GATATCAAGC CGGATGGAAA ACGCCATGCC
 601  GTCATCAGCG GTTCCGTCCT TTACAACCAA GCCGAGAAAG GCAGTTACTC
 651  CCTCGGTATC TTTGGCGGAA AAGCCCAGGA AGTTGCCGGC AGCGCGGAAG
 701  TGAAAACCGT AAACGGCATA CGCCATATCG GCCTTGCCGC CAAGCAACTC
 751  GAGGGTGGCG GAGGCACTGG ATCCGCCACA AACGACGACG ATGTTAAAAA
 801  AGCTGCCACT GTGGCCATTG CTGCTGCCTA CAACAATGGC CAAGAAATCA
 851  ACGGTTTCAA AGCTGGAGAG ACCATCTACG ACATTGATGA AGACGGCACA
 901  ATTACCAAAA AAGACGCAAC TGCAGCCGAT GTTGAAGCCG ACGACTTTAA
 951  AGGTCTGGGT CTGAAAAAAG TCGTGACTAA CCTGACCAAA ACCGTCAATG
1001  AAAACAAACA AAACGTCGAT GCCAAAGTAA AAGCTGCAGA ATCTGAAATA
1051  GAAAAGTTAA CAACCAAGTT AGCAGACACT GATGCCGCTT TAGCAGATAC
1101  TGATGCCGCT CTGGATGCAA CCACCAACGC CTTGAATAAA TTGGGAGAAA
1151  ATATAACGAC ATTTGCTGAA GAGACTAAGA CAAATATCGT AAAAATTGAT
1201  GAAAAATTAG AAGCCGTGGC TGATACCGTC GACAAGCATG CCGAAGCATT
1251  CAACGATATC GCCGATTCAT TGGATGAAAC CAACACTAAG GCAGACGAAG
1301  CCGTCAAAAC CGCCAATGAA GCCAAACAGA CGGCCGAAGA AACCAAACAA
1351  AACGTCGATG CCAAAGTAAA AGCTGCAGAA ACTGCAGCAG GCAAAGCCGA
1401  AGCTGCCGCT GGCACAGCTA ATACTGCAGC CGACAAGGCC GAAGCTGTCG
1451  CTGCAAAAGT TACCGACATC AAAGCTGATA TCGCTACGAA CAAAGATAAT
1501  ATTGCTAAAA AAGCAAACAG TGCCGACGTG TACACCAGAG AAGAGTCTGA
1551  CAGCAAATTT GTCAGAATTG ATGGTCTGAA CGCTACTACC GAAAAATTGG
1601  ACACACGCTT GGCTTCTGCT GAAAAATCCA TTGCCGATCA CGATACTCGC
1651  CTGAACGGTT TGGATAAAAC AGTGTCAGAC CTGCGCAAAG AAACCCGCCA
1701  AGGCCTTGCA GAACAAGCCG CGCTCTCCGG TCTGTTCCAA CCTTACAACG
1751  TGGGTCGGTT CAATGTAACG GCTGCAGTCG GCGGCTACAA ATCCGAATCG
1801  GCAGTCGCCA TCGGTACCGG CTTCCGCTTT ACCGAAAACT TTGCCGCCAA
1851  AGCAGGCGTG GCAGTCGGCA CTTCGTCCGG TTCTTCCGCA GCCTACCATG
1901  TCGGCGTCAA TTACGAGTGG CTCGAGCACC ACCACCACCA CCACTGA
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   1  MVAADIGAGL ADALTAPLDH KDKGLQSLTL DQSVRKNEKL KLAAQGAEKT
  51  YGNGDSLNTG KLKNDKVSRF DFIRQIEVDG QLITLESGEF QVYKQSHSAL
 101  TAFQTEQIQD SEHSGKMVAK RQFRIGDIAG EHTSFDKLPE GGRATYRGTA
 151  FGSDDAGGKL TYTIDFAAKQ GNGKIEHLKS PELNVDLAAA DIKPDGKRHA
 201  VISGSVLYNQ AEKGSYSLGI FGGKAQEVAG SAEVKTVNGI RHIGLAAKQL
 251  EGGGGTGSAT NDDDVKKAAT VAIAAAYNNG QEINGFKAGE TIYDIDEDGT
 301  ITKKDATAAD VEADDFKGLG LKKVVTNLTK TVNENKQNVD AKVKAAESEI
 351  EKLTTKLADT DAALADTDAA LDATTNALNK LGENITTFAE ETKTNIVKID
 401  EKLEAVADTV DKHAEAFNDI ADSLDETNTK ADEAVKTANE AKQTAEETKQ
 451  NVDAKVKAAE TAAGKAEAAA GTANTAADKA EAVAAKVTDI KADIATNKDN
 501  IAKKANSADV YTREESDSKF VRIDGLNATT EKLDTRLASA EKSIADHDTR
 551  LNGLDKTVSD LRKETRQGLA EQAALSGLFQ PYNVGRFNVT AAVGGYKSES
 601  AVAIGTGFRF TENFAAKAGV AVGTSSGSSA AYHVGVNYEW LEHHHHHH*
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ΔG741−961c

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   1  ATGGTCGCCG CCGACATCGG TGCGGGGCTT GCCGATGCAC TAACCGCACC
  51  GCTCGACCAT AAAGACAAAG GTTTGCAGTC TTTGACGCTG GATCAGTCCG
 101  TCAGGAAAAA CGAGAAACTG AAGCTGGCGG CACAAGGTGC GGAAAAAACT
 151  TATGGAAACG GTGACAGCCT CAATACGGGC AAATTGAAGA ACGACAAGGT
 201  CAGCCGTTTC GACTTTATCC GCCAAATCGA AGTGGACGGG CAGCTCATTA
 251  CCTTGGAGAG TGGAGAGTTC CAAGTATACA AACAAAGCCA TTCCGCCTTA
 301  ACCGCCTTTC AGACCGAGCA AATACAAGAT TCGGAGCATT CCGGGAAGAT
 351  GGTTGCGAAA CGCCAGTTCA GAATCGGCGA CATAGCGGGC GAACATACAT
 401  CTTTTGACAA GCTTCCCGAA GGCGGCAGGG CGACATATCG CGGGACGGCG
 451  TTCGGTTCAG ACGATGCCGG CGGAAAACTG ACCTACACCA TAGATTTCGC
 501  CGCCAAGCAG GGAAACGGCA AAATCGAACA TTTGAAATCG CCAGAACTCA
 551  ATGTCGACCT GGCCGCCGCC GATATCAAGC CGGATGGAAA ACGCCATGCC
 601  GTCATCAGCG GTTCCGTCCT TTACAACCAA GCCGAGAAAG GCAGTTACTC
 651  CCTCGGTATC TTTGGCGGAA AAGCCCAGGA AGTTGCCGGC AGCGCGGAAG
 701  TGAAAACCGT AAACGGCATA CGCCATATCG GCCTTGCCGC CAAGCAACTC
 751  GAGGGTGGCG GAGGCACTGG ATCCGCCACA AACGACGACG ATGTTAAAAA
 801  AGCTGCCACT GTGGCCATTG CTGCTGCCTA CAACAATGGC CAAGAAATCA
 851  ACGGTTTCAA AGCTGGAGAG ACCATCTACG ACATTGATGA AGACGGCACA
 901  ATTACCAAAA AAGACGCAAC TGCAGCCGAT GTTGAAGCCG ACGACTTTAA
 951  AGGTCTGGGT CTGAAAAAAG TCGTGACTAA CCTGACCAAA ACCGTCAATG
1001  AAAACAAACA AAACGTCGAT GCCAAAGTAA AAGCTGCAGA ATCTGAAATA
1051  GAAAAGTTAA CAACCAAGTT AGCAGACACT GATGCCGCTT TAGCAGATAC
1101  TGATGCCGCT CTGGATGCAA CCACCAACGC CTTGAATAAA TTGGGAGAAA
1151  ATATAACGAC ATTTGCTGAA GAGACTAAGA CAAATATCGT AAAAATTGAT
1201  GAAAAATTAG AAGCCGTGGC TGATACCGTC GACAAGCATG CCGAAGCATT
1251  CAACGATATC GCCGATTCAT TGGATGAAAC CAACACTAAG GCAGACGAAG
1301  CCGTCAAAAC CGCCAATGAA GCCAAACAGA CGGCCGAAGA AACCAAACAA
1351  AACGTCGATG CCAAAGTAAA AGCTGCAGAA ACTGCAGCAG GCAAAGCCGA
1401  AGCTGCCGCT GGCACAGCTA ATACTGCAGC CGACAAGGCC GAAGCTGTCG
1451  CTGCAAAAGT TACCGACATC AAAGCTGATA TCGCTACGAA CAAAGATAAT
1501  ATTGCTAAAA AAGCAAACAG TGCCGACGTG TACACCAGAG AAGAGTCTGA
1551  CAGCAAATTT GTCAGAATTG ATGGTCTGAA CGCTACTACC GAAAAATTGG
1601  ACACACGCTT GGCTTCTGCT GAAAAATCCA TTGCCGATCA CGATACTCGC
1651  CTGAACGGTT TGGATAAAAC AGTGTCAGAC CTGCGCAAAG AAACCCGCCA
1701  AGGCCTTGCA GAACAAGCCG CGCTCTCCGG TCTGTTCCAA CCTTACAACG
1751  TGGGTCTCGA GCACCACCAC CACCACCACT GA
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   1  MVAADIGAGL ADALTAPLDH KDKGLQSLTL DQSVRKNEKL KLAAQGAEKT
  51  YGNGDSLNTG KLKNDKVSRF DFIRQIEVDG QLITLESGEF QVYKQSHSAL
 101  TAFQTEQIQD SEHSGKMVAK RQFRIGDIAG EHTSFDKLPE GGRATYRGTA
 151  FGSDDAGGKL TYTIDFAAKQ GNGKIEHLKS PELNVDLAAA DIKPDGKRHA
 201  VISGSVLYNQ AEKGSYSLGI FGGKAQEVAG SAEVKTVNGI RHIGLAAKQL
 251  EGGGGTGSAT NDDDVKKAAT VAIAAAYNNG QEINGFKAGE TIYDIDEDGT
 301  ITKKDATAAD VEADDFKGLG LKKVVTNLTK TVNENKQNVD AKVKAAESEI
 351  EKLTTKLADT DAALADTDAA LDATTNALNK LGENITTFAE ETKTNIVKID
 401  EKLEAVADTV DKHAEAFNDI ADSLDETNTK ADEAVKTANE AKQTAEETKQ
 451  NVDAKVKAAE TAAGKAEAAA GTANTAADKA EAVAAKVTDI KADIATNKDN
 501  IAKKANSADV YTREESDSKF VRIDGLNATT EKLDTRLASA EKSIADHDTR
 551  LNGLDKTVSD LRKETRQGLA EQAALSGLFQ PYNVGLEHHH HHH*
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ΔG741-983

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   1  ATGGTCGCCG CCGACATCGG TGCGGGGCTT GCCGATGCAC TAACCGCACC
  51  GCTCGACCAT AAAGACAAAG GTTTGCAGTC TTTGACGCTG GATCAGTCCG
 101  TCAGGAAAAA CGAGAAACTG AAGCTGGCGG CACAAGGTGC GGAAAAAACT
 151  TATGGAAACG GTGACAGCCT CAATACGGGC AAATTGAAGA ACGACAAGGT
 201  CAGCCGTTTC GACTTTATCC GCCAAATCGA AGTGGACGGG CAGCTCATTA
 251  CCTTGGAGAG TGGAGAGTTC CAAGTATACA AACAAAGCCA TTCCGCCTTA
 301  ACCGCCTTTC AGACCGAGCA AATACAAGAT TCGGAGCATT CCGGGAAGAT
 351  GGTTGCGAAA CGCCAGTTCA GAATCGGCGA CATAGCGGGC GAACATACAT
 401  CTTTTGACAA GCTTCCCGAA GGCGGCAGGG CGACATATCG CGGGACGGCG
 451  TTCGGTTCAG ACGATGCCGG CGGAAAACTG ACCTACACCA TAGATTTCGC
 501  CGCCAAGCAG GGAAACGGCA AAATCGAACA TTTGAAATCG CCAGAACTCA
 551  ATGTCGACCT GGCCGCCGCC GATATCAAGC CGGATGGAAA ACGCCATGCC
 601  GTCATCAGCG GTTCCGTCCT TTACAACCAA GCCGAGAAAG GCAGTTACTC
 651  CCTCGGTATC TTTGGCGGAA AAGCCCAGGA AGTTGCCGGC AGCGCGGAAG
 701  TGAAAACCGT AAACGGCATA CGCCATATCG GCCTTGCCGC CAAGCAACTC
 751  GAGGGATCCG GCGGAGGCGG CACTTCTGCG CCCGACTTCA ATGCAGGCGG
 801  TACCGGTATC GGCAGCAACA GCAGAGCAAC AACAGCGAAA TCAGCAGCAG
 851  TATCTTACGC CGGTATCAAG AACGAAATGT GCAAAGACAG AAGCATGCTC
 901  TGTGCCGGTC GGGATGACGT TGCGGTTACA GACAGGGATG CCAAAATCAA
 951  TGCCCCCCCC CCGAATCTGC ATACCGGAGA CTTTCCAAAC CCAAATGACG
1001  CATACAAGAA TTTGATCAAC CTCAAACCTG CAATTGAAGC AGGCTATACA
1051  GGACGCGGGG TAGAGGTAGG TATCGTCGAC ACAGGCGAAT CCGTCGGCAG
1101  CATATCCTTT CCCGAACTGT ATGGCAGAAA AGAACACGGC TATAACGAAA
1151  ATTACAAAAA CTATACGGCG TATATGCGGA AGGAAGCGCC TGAAGACGGA
1201  GGCGGTAAAG ACATTGAAGC TTCTTTCGAC GATGAGGCCG TTATAGAGAC
1251  TGAAGCAAAG CCGACGGATA TCCGCCACGT AAAAGAAATC GGACACATCG
1301  ATTTGGTCTC CCATATTATT GGCGGGCGTT CCGTGGACGG CAGACCTGCA
1351  GGCGGTATTG CGCCCGATGC GACGCTACAC ATAATGAATA CGAATGATGA
1401  AACCAAGAAC GAAATGATGG TTGCAGCCAT CCGCAATGCA TGGGTCAAGC
1451  TGGGCGAACG TGGCGTGCGC ATCGTCAATA ACAGTTTTGG AACAACATCG
1501  AGGGCAGGCA CTGCCGACCT TTTCCAAATA GCCAATTCGG AGGAGCAGTA
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1551   CCGCCAAGCG TTGCTCGACT ATTCCGGCGG TGATAAAACA GACGAGGGTA
1601   TCCGCCTGAT GCAACAGAGC GATTACGGCA ACCTGTCCTA CCACATCCGT
1651   AATAAAAACA TGCTTTTCAT CTTTTCGACA GGCAATGACG CACAAGCTCA
1701   GCCCAACACA TATGCCCTAT TGCCATTTTA TGAAAAAGAC GCTCAAAAAG
1751   GCATTATCAC AGTCGCAGGC GTAGACCGCA GTGGAGAAAA GTTCAAACGG
1801   GAAATGTATG GAGAACCGGG TACAGAACCG CTTGAGTATG GCTCCAACCA
1851   TTGCGGAATT ACTGCCATGT GGTGCCTGTC GGCACCCTAT GAAGCAAGCG
1901   TCCGTTTCAC CCGTACAAAC CCGATTCAAA TTGCCGGAAC ATCCTTTTCC
1951   GCACCCATCG TAACCGGCAC GGCGGCTCTG CTGCTGCAGA AATACCCGTG
2001   GATGAGCAAC GACAACCTGC GTACCACGTT GCTGACGACG GCTCAGGACA
2051   TCGGTGCAGT CGGCGTGGAC AGCAAGTTCG GCTGGGGACT GCTGGATGCG
2101   GGTAAGGCCA TGAACGGACC CGCGTCCTTT CCGTTCGGCG ACTTTACCGC
2151   CGATACGAAA GGTACATCCG ATATTGCCTA CTCCTTCCGT AACGACATTT
2201   CAGGCACGGG CGGCCTGATC AAAAAAGGCG GCAGCCAACT GCAACTGCAC
2251   GGCAACAACA CCTATACGGG CAAAACCATT ATCGAAGGCG GTTCGCTGGT
2301   GTTGTACGGC AACAACAAAT CGGATATGCG CGTCGAAACC AAAGGTGCGC
2351   TGATTTATAA CGGGGCGGCA TCCGGCGGCA GCCTGAACAG CGACGGCATT
2401   GTCTATCTGG CAGATACCGA CCAATCCGGC GCAAACGAAA CCGTACACAT
2451   CAAAGGCAGT CTGCAGCTGG ACGGCAAAGG TACGCTGTAC ACACGTTTGG
2501   GCAAACTGCT GAAAGTGGAC GGTACGGCGA TTATCGGCGG CAAGCTGTAC
2551   ATGTCGGCAC GCGGCAAGGG GGCAGGCTAT CTCAACAGTA CCGGACGACG
2601   TGTTCCCTTC CTGAGTGCCG CCAAAATCGG GCAGGATTAT TCTTTCTTCA
2651   CAAACATCGA AACCGACGGC GGCCTGCTGG CTTCCCTCGA CAGCGTCGAA
2701   AAAACAGCGG GCAGTGAAGG CGACACGCTG TCCTATTATG TCCGTCGCGG
2751   CAATGCGGCA CGGACTGCTT CGGCAGCGGC ACATTCCGCG CCCGCCGGTC
2801   TGAAACACGC CGTAGAACAG GGCGGCAGCA ATCTGGAAAA CCTGATGGTC
2851   GAACTGGATG CCTCCGAATC ATCCGCAACA CCCGAGACGG TTGAAACTGC
2901   GGCAGCCGAC CGCACAGATA TGCCGGGCAT CCGCCCCTAC GGCGCAACTT
2951   TCCGCGCAGC GGCAGCCGTA CAGCATGCGA ATGCCGCCGA CGGTGTACGC
3001   ATCTTCAACA GTCTCGCCGC TACCGTCTAT GCCGACAGTA CCGCCGCCCA
3051   TGCCGATATG CAGGGACGCC GCCTGAAAGC CGTATCGGAC GGGTTGGACC
3101   ACAACGGCAC GGGTCTGCGC GTCATCGCGC AAACCCAACA GGACGGTGGA
3151   ACGTGGGAAC AGGGCGGTGT TGAAGGCAAA ATGCGCGGCA GTACCCAAAC
3201   CGTCGGCATT GCCGCGAAAA CCGGCGAAAA TACGACAGCA GCCGCCACAC
3251   TGGGCATGGG ACGCAGCACA TGGAGCGAAA ACAGTGCAAA TGCAAAAACC
3301   GACAGCATTA GTCTGTTTGC AGGCATACGG CACGATGCGG GCGATATCGG
3351   CTATCTCAAA GGCCTGTTCT CCTACGGACG CTACAAAAAC AGCATCAGCC
3401   GCAGCACCGG TGCGGACGAA CATGCGGAAG GCAGCGTCAA CGGCACGCTG
3451   ATGCAGCTGG GCGCACTGGG CGGTGTCAAC GTTCCGTTTG CCGCAACGGG
3501   AGATTTGACG GTCGAAGGCG GTCTGCGCTA CGACCTGCTC AAACAGGATG
3551   CATTCGCCGA AAAAGGCAGT GCTTTGGGCT GGAGCGGCAA CAGCCTCACT
3601   GAAGGCACGC TGGTCGGACT CGCGGGTCTG AAGCTGTCGC AACCCTTGAG
3651   CGATAAAGCC GTCCTGTTTG CAACGGCGGG CGTGGAACGC GACCTGAACG
3701   GACGCGACTA CACGGTAACG GGCGGCTTTA CCGGCGCGAC TGCAGCAACC
3751   GGCAAGACGG GGGCACGCAA TATGCCGCAC ACCCGTCTGG TTGCCGGCCT
3801   GGGCGCGGAT GTCGAATTCG GCAACGGCTG GAACGGCTTG GCACGTTACA
3851   GCTACGCCGG TTCCAAACAG TACGGCAACC ACAGCGGACG AGTCGGCGTA
3901   GGCTACCGGT TCCTCGAGCA CCACCACCAC CACCACTGA
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   1 MVAADIGAGL ADALTAPLDH KDKGLQSLTL DQSVRKNEKL KLAAQGAEKT
  51 YGNGDSLNTG KLKNDKVSRF DFIRQIEVDG QLITLESGEF QVYKQSHSAL
 101 TAFQTEQIQD SEHSGKMVAK RQFRIGDIAG EHTSFDKLPE GGRATYRGTA
 151 FGSDDAGGKL TYTIDFAAKQ GNGKIEHLKS PELNVDLAAA DIKPDGKRHA
 201 VISGSVLYNQ AEKGSYSLGI FGGKAQEVAG SAEVKTVNGI RHIGLAAKQL
 251 EGSGGGGTSA PDFNAGGTGI GSNSRATTAK SAAVSYAGIK NEMCKDRSML
 301 CAGRDDVAVT DRDAKINAPP PNLHTGDFPN PNDAYKNLIN LKPAIEAGYT
 351 GRGVEVGIVD TGESVGSISF PELYGRKEHG YNENYKNYTA YMRKEAPEDG
 401 GGKDIEASFD DEAVIETEAK PTDIRHVKEI GHIDLVSHII GGRSVDGRPA
 451 GGIAPDATLH IMNTNDETKN EMMVAAIRNA WVKLGERGVR IVNNSFGTTS
 501 RAGTADLFQI ANSEEQYRQA LLDYSGGDKT DEGIRLMQQS DYGNLSYHIR
 551 NKNMLFIFST GNDAQAQPNT YALLPFYEKD AQKGIITVAG VDRSGEKFKR
 601 EMYGEPGTEP LEYGSNHCGI TAMWCLSAPY EASVRFTRTN PIQIAGTSFS
 651 APIVTGTAAL LLQKYPWMSN DNLRTTLLTT AQDIGAVGVD SKFGWGLLDA
 701 GKAMNGPASF PFGDFTADTK GTSDIAYSFR NDISGTGGLI KKGGSQLQLH
 751 GNNTYTGKTI IEGGSLVLYG NNKSDMRVET KGALIYNGAA SGGSLNSDGI
 801 VYLADTDQSG ANETVHIKGS LQLDGKGTLY TRLGKLLKVD GTAIIGGKLY
 851 MSARGKGAGY LNSTGRRVPF LSAAKIGQDY SFFTNIETDG GLLASLDSVE
 901 KTAGSEGDTL SYYVRRGNAA RTASAAAHSA PAGLKHAVEQ GGSNLENLMV
 951 ELDASESSAT PETVETAAAD RTDMPGIRPY GATFRAAAAV QHANAADGVR
1001 IFNSLAATVY ADSTAAHADM QGRRLKAVSD GLDHNGTGLR VIAQTQQDGG
1051 TWEQGGVEGK MRGSTQTVGI AAKTGENTTA AATLGMGRST WSENSANAKT
1101 DSISLFAGIR HDAGDIGYLK GLFSYGRYKN SISRSTGADE HAEGSVNGTL
1151 MQLGALGGVN VPFAATGDLT VEGGLRYDLL KQDAFAEKGS ALGWSGNSLT
1201 EGTLVGLAGL KLSQPLSDKA VLFATAGVER DLNGRDYTVT GGFTGATAAT
1251 GKTGARNMPH TRLVAGLGAD VEFGNGWNGL ARYSYAGSKQ YGNHSGRVGV
1301 GYRFLEHHHH HH*
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ΔG741–ORF46.1

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   1 ATGGTCGCCG CCGACATCGG TGCGGGGCTT GCCGATGCAC TAACCGCACC
  51 GCTCGACCAT AAAGACAAAG GTTTGCAGTC TTTGACGCTG GATCAGTCCG
 101 TCAGGAAAAA CGAGAAACTG AAGCTGGCGG CACAAGGTGC GGAAAAAACT
 151 TATGGAAACG GTGACAGCCT CAATACGGGC AAATTGAAGA ACGACAAGGT
 201 CAGCCGTTTC GACTTTATCC GCCAAATCGA AGTGGACGGG CAGCTCATTA
 251 CCTTGGAGAG TGGAGAGTTC CAAGTATACA AACAAAGCCA TTCCGCCTTA
 301 ACCGCCTTTC AGACCGAGCA AATACAAGAT TCGGAGCATT CCGGGAAGAT
 351 GGTTGCGAAA CGCCAGTTCA GAATCGGCGA CATAGCGGGC GAACATACAT
 401 CTTTTGACAA GCTTCCCGAA GGCGGCAGGG CGACATATCG CGGGACGGCG
 451 TTCGGTTCAG ACGATGCCGG CGGAAAACTG ACCTACACCA TAGATTTCGC
 501 CGCCAAGCAG GGAAACGGCA AAATCGAACA TTTGAAATCG CCAGAACTCA
 551 ATGTCGACCT GGCCGCCGCC GATATCAAGC CGGATGGAAA ACGCCATGCC
 601 GTCATCAGCG GTTCCGTCCT TTACAACCAA GCCGAGAAAG GCAGTTACTC
 651 CCTCGGTATC TTTGGCGGAA AAGCCCAGGA AGTTGCCGGC AGCGCGGAAG
 701 TGAAAACCGT AAACGGCATA CGCCATATCG GCCTTGCCGC CAAGCAACTC
 751 GACGGTGGCG GAGGCACTGG ATCCTCAGAT TTGGCAAACG ATTCTTTTAT
 801 CCGGCAGGTT CTCGACCGTC AGCATTTCGA ACCCGACGGG AAATACCACC
 851 TATTCGGCAG CAGGGGGGAA CTTGCCGAGC GCAGCGGCCA TATCGGATTG
 901 GGAAAAATAC AAAGCCATCA GTTGGGCAAC CTGATGATTC AACAGGCGGC
 951 CATTAAAGGA AATATCGGCT ACATTGTCCG CTTTTCCGAT CACGGGCACG
1001 AAGTCCATTC CCCCTTCGAC AACCATGCCT CACATTCCGA TTCTGATGAA
1051 GCCGGTAGTC CCGTTGACGG ATTTAGCCTT TACCGCATCC ATTGGGACGG
1101 ATACGAACAC CATCCCGCCG ACGGCTATGA CGGGCCACAG GGCGGCGGCT
1151 ATCCCGCTCC CAAAGGCGCG AGGGATATAT ACAGCTACGA CATAAAAGGC
1201 GTTGCCCAAA ATATCCGCCT CAACCTGACC GACAACCGCA GCACCGGACA
1251 ACGGCTTGCC GACCGTTTCC ACAATGCCGG TAGTATGCTG ACGCAAGGAG
1301 TAGGCGACGG ATTCAAACGC GCCACCCGAT ACAGCCCCGA GCTGGACAGA
1351 TCGGGCAATG CCGCCGAAGC CTTCAACGGC ACTGCAGATA TCGTTAAAAA
1401 CATCATCGGC GCGGCAGGAG AAATTGTCGG CGCAGGCGAT GCCGTGCAGG
1451 GCATAAGCGA AGGCTCAAAC ATTGCTGTCA TGCACGGCTT GGGTCTGCTT
1501 TCCACCGAAA ACAAGATGGC GCGCATCAAC GATTTGGCAG ATATGGCGCA
1551 ACTCAAAGAC TATGCCGCAG CAGCCATCCG CGATTGGGCA GTCCAAAACC
1601 CCAATGCCGC ACAAGGCATA GAAGCCGTCA GCAATATCTT TATGGCAGCC
1651 ATCCCCATCA AAGGGATTGG AGCTGTTCGG GGAAAATACG GCTTGGGCGG
1701 CATCACGGCA CATCCTATCA AGCGGTCGCA GATGGGCGCG ATCGCATTGC
1751 CGAAAGGGAA ATCCGCCGTC AGCGACAATT TTGCCGATGC GGCATACGCC
1801 AAATACCCGT CCCCTTACCA TTCCCGAAAT ATCCGTTCAA ACTTGGAGCA
1851 GCGTTACGGC AAAGAAAACA TCACCTCCTC AACCGTGCCG CCGTCAAACG
1901 GCAAAAATGT CAAACTGGCA GACCAACGCC ACCCGAAGAC AGGCGTACCG
1951 TTTGACGGTA AAGGGTTTCC GAATTTTGAG AAGCACGTGA AATATGATAC
2001 GCTCGAGCAC CACCACCACC ACCACTGA
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   1 MVAADIGAGL ADALTAPLDH KDKGLQSLTL DQSVRKNEKL KLAAQGAEKT
  51 YGNGDSLNTG KLKNDKVSRF DFIRQIEVDG QLITLESGEF QVYKQSHSAL
 101 TAFQTEQIQD SEHSGKMVAK RQFRIGDIAG EHTSFDKLPE GGRATYRGTA
 151 FGSDDAGGKL TYTIDFAAKQ GNGKIEHLKS PELNVDLAAA DIKPDGKRHA
 201 VISGSVLYNQ AEKGSYSLGI FGGKAQEVAG SAEVKTVNGI RHIGLAAKQL
 251 DGGGGTGSSD LANDSFIRQV LDRQHFEPDG KYHLFGSRGE LAERSGHIGL
 301 GKIQSHQLGN LMIQQAAIKG NIGYIVRFSD HGHEVHSPFD NHASHSDSDE
 351 AGSPVDGFSL YRIHWDGYEH HPADGYDGPQ GGGYPAPKGA RDIYSYDIKG
 401 VAQNIRLNLT DNRSTGQRLA DRFHNAGSML TQGVGDGFKR ATRYSPELDR
 451 SGNAAEAFNG TADIVKNIIG AAGEIVGAGD AVQGISEGSN IAVMHGLGLL
 501 STENKMARIN DLADMAQLKD YAAAAIRDWA VQNPNAAQGI EAVSNIFMAA
 551 IPIKGIGAVR GKYGLGGITA HPIKRSQMGA IALPKGKSAV SDNFADAAYA
 601 KYPSPYHSRN IRSNLEQRYG KENITSSTVP PSNGKNVKLA DQRHPKTGVP
 651 FDGKGFPNFE KHVKYDTLEH HHHHH*
```

Example 16 - C-terminal fusions ('hybrids') with 287/ΔG287

[0228] According to the invention, hybrids of two proteins A & B may be either NH_2-A-B-COOH or NH_2-B-A-COOH. The effect of this difference was investigated using protein 287 either C-terminal (in '287-His' form) or N-terminal (in

ΔG287 form - sequences shown above) to 919, 953 and ORF46.1. A panel of strains was used, including homologous strain 2996. FCA was used as adjuvant:

	287 & 919		287 & 953		287 & ORF46.1	
Strain	*ΔG287-919*	*919-287*	*ΔG287-953*	*953-287*	*ΔG287-46.1*	*46.1-287*
2996	128000	16000	65536	8192	16384	8192
BZ232	256	128	128	<4	<4	<4
1000	2048	<4	<4	<4	<4	<4
MC58	8192	1024	16384	1024	512	128
NGH38	32000	2048	>2048	4096	16384	4096
394/98	4096	32	256	128	128	16
MenA (F6124)	32000	2048	>2048	32	8192	1024
MenC (BZ133)	64000	>8192	>8192	<16	8192	2048

Better bactericidal titres are generally seen with 287 at the N-terminus (in the ΔG form)

[0229] When fused to protein 961 [NH_2-ΔG287-961-COOH - sequence shown above], the resulting protein is insoluble and must be denatured and renatured for purification. Following renaturation, around 50% of the protein was found to remain insoluble. The soluble and insoluble proteins were compared, and much better bactericidal titres were obtained with the soluble protein (FCA as adjuvant):

	2996	BZ232	MC58	NGH38	F6124	BZ133
Soluble	65536	128	4096	>2048	>2048	4096
Insoluble	8192	<4	<4	16	n.d.	n.d.

[0230] Titres with the insoluble form were, however, improved by using alum adjuvant instead:

Insoluble	32768	1128	4096	>2048	>2048	2048

Example 17 — N-terminal fusions ('hybrids') to 287

[0231] Expression of protein 287 as full-length with a C-terminal His-tag, or without its leader peptide but with a C-terminal His-tag, gives fairly low expression levels. Better expression is achieved using a N-terminal GST-fusion.

[0232] As an alternative to using GST as an N-terminal fusion partner, 287 was placed at the C-terminus of protein 919 ('919-287'), of protein 953 ('953-287'), and of proteins ORF46.1 ('ORF46.1-287'). In both cases, the leader peptides were deleted, and the hybrids were direct in-frame fusions.

[0233] To generate the 953-287 hybrid, the leader peptides of the two proteins were omitted by designing the forward primer downstream from the leader of each sequence; the stop codon sequence was omitted in the 953 reverse primer but included in the 287 reverse primer. For the 953 gene, the 5' and the 3' primers used for amplification included a *Nde*I and a *Bam*HI restriction sites respectively, whereas for the amplification of the 287 gene the 5' and the 3' primers included a *Bam*HI and a *Xho*I restriction sites respectively. In this way a sequential directional cloning of the two genes in pET21b+, using *Nde*I-*Bam*HI (to clone the first gene) and subsequently *Bam*HI-*Xho*I (to clone the second gene) could be achieved.

[0234] The 919-287 hybrid was obtained by cloning the sequence coding for the mature portion of 287 into the *Xho*I site at the 3'-end of the 919-His clone in pET21b+. The primers used for amplification of the 287 gene were designed for introducing a *Sal*I restriction site at the 5'-and a *Xho*I site at the 3'- of the PCR fragment. Since the cohesive ends produced by the *Sal*I and *Xho*I restriction enzymes are compatible, the 287 PCR product digested with *Sal*I-*Xho*I could be inserted in the pET21 b-919 clone cleaved with *Xho*I.

[0235] The ORF46.1-287 hybrid was obtained similarly.

[0236] The bactericidal efficacy (homologous strain) of antibodies raised against the hybrid proteins was compared

with antibodies raised against simple mixtures of the component antigens:

	Mixture with 287	Hybrid with 287
919	32000	16000
953	8192	8192
ORF46.1	128	8192

[0237] Data for bactericidal activity against heterologous MenB strains and against serotypes A and C were also obtained for 919-287 and 953-287:

	919		953		ORF46.1	
Strain	*Mixture*	*Hybrid*	*Mixture*	*Hybrid*	*Mixture*	*Hybrid*
MC58	512	1024	512	1024	-	1024
NGH38	1024	2048	2048	4096	-	4096
BZ232	512	128	1024	16	-	-
MenA (F6124)	512	2048	2048	32	-	1024
MenC (C11)	>2048	n.d.	>2048	n.d.	-	n.d.
MenC (BZ133)	>4096	>8192	>4096	<16	-	2048

[0238] Hybrids of ORF46.1 and 919 were also constructed. Best results (four-fold higher titre) were achieved with 919 at the N-terminus.

[0239] Hybrids 919-519His, ORF97-225His and 225-ORF97His were also tested. These gave moderate ELISA fitres and bactericidal antibody responses.

Example 18 - the leader peptide from ORF4

[0240] As shown above, the leader peptide of ORF4 can be fused to the mature sequence of other proteins (e.g. proteins 287 and 919). It is able to direct lipidation in *E.coli.*

Example 19 - domains in 564

[0241] The protein '564' is very large (2073aa), and it is difficult to clone and express it in complete form. To facilitate expression, the protein has been divided into four domains, as shown in figure 8 (according to the MC58 sequence):

Domain	A	B	C	D
Amino Acids	79-360	361-731	732-2044	2045-2073

[0242] These domains show the following homologies:

- Domain A shows homology to other bacterial toxins:

  gb|AAG03431.1|AE004443_9probable hemagglutinin [Pseudomonas aeruginosa] (38%)
  gb|AAC31981.1| (139897) HecA [Pectobacterium chrysanthemi] (45%)
  emb|CAA36409.1| (X52156) filamentous hemagglutinin [Bordetella pertussis] (31%)
  gb|AAC79757.1| (AF057695) large supernatant protein1 [Haemophilus ducreyi] (26%)
  gb|AAA25657.1| (M30186) HpmA precursor [Proteus mirabilis] (29%)

- Domain B shows no homology, and is specific to 564.
- Domain C shows homology to:

gb|AAF84995.1|AE004032 HA-like secreted protein [Xylella fastidiosa] (33%)
gb|AAG05850.1|AE004673 hypothetical protein [Pseudomonas aeruginosa] (27%)
gb|AAF68414.1AF237928 putative FHA [Pasteurella multocisìda] (23%)
gb|AAC79757.1|(AF057695) large supernatant protein1 [Haemophilus ducreyi] (23%)
pir||S21010 FHA B precursor [Bordetella pertussis] (20%)

- Domain D shows homology to other bacterial toxins:

  gb|AAF84995.1|AE004032_14 HA-like secreted protein [Xylella fastidiosa] (29%)

[0243] Using the MC58 strain sequence, good intracellular expression of 564ab was obtained in the form of GST-fusions (no purification) and his-tagged protein; this domain-pair was also expressed as a lipoprotein, which showed moderate expression in the outer membrane/supernatant fraction.
[0244] The b domain showed moderate intracellular expression when expressed as a his-tagged product (no purification), and good expression as a GST-fusion.
[0245] The c domain showed good intracellular expression as a GST-fusion, but was insoluble. The d domain showed moderate intracellular expression as a his-tagged product (no purification). The cd protein domain-pair showed moderate intracellular expression (no purification) as a GST-fusion.
[0246] Good bactericidal assay titres were observed using the c domain and the bc pair.

Example 20 - the 919 leader peptide

[0247] The 20mer leader peptide from 919 is discussed in example 1 above:
MKKYLFRAAL YGIAAAILAA
[0248] As shown in example 1, deletion of this leader improves heterologous expression, as does substitution with the ORF4 leader peptide. The influence of the 919 leader on expression was investigated by fusing the coding sequence to the *PhoC* reporter gene from *Morganella morganii* [Thaller et al. (1994) Microbiology 140:1341-1350]. The construct was cloned in the pET21-b plasmid between the *Nde*I and *Xho*I sites (Figure 9):

```
  1  MKKYLFRAAL YGIAAAILAA AIPAGNDATT KPDLYYLKNE QAIDSLKLLP
 51  PPPEVGSIQF LNDQAMYEKG RMLRNTERGK QAQADADLAA GGVATAFSGA
101  FGYPITEKDS PELYKLLTNM IEDAGDLATR SAKEHYMRIR PFAFYGTETC
151  NTKDQKKLST NGSYPSGHTS IGWATALVLA EVNPANQDAI LERGYQLGQS
201  RVICGYHWQS DVDAARIVGS AAVATLHSDP AFQAQLAKAK QEFAQKSQK*
```

[0249] The level of expression of PhoC from this plasmid is >200-fold lower than that found for the same construct but containing the native PhoC signal peptide. The same result was obtained even after substitution of the T7 promoter with the *E.coli* Plac promoter. This means that the influence of the 919 leader sequence on expression does not depend on the promoter used.
[0250] In order to investigate if the results observed were due to some peculiarity of the 919 signal peptide nucleotide sequence (secondary structure formation, sensitivity to RNAases, *etc.*) or to protein instability induced by the presence of this signal peptide, a number of mutants were generated. The approach used was a substitution of nucleotides of the 919 signal peptide sequence by cloning synthetic linkers containing degenerate codons. In this way, mutants were obtained with nucleotide and/or amino acid substitutions.
[0251] Two different linkers were used, designed to produce mutations in two different regions of the 919 signal peptide sequence, in the first 19 base pairs (L1) and between bases 20-36 (S1).

L1: 5′ T ATG AAa/g TAc/t c/tTN TTt/c a/cGC GCC GCC CTG TAC GGC ATC GCC GCC GCC ATC CTC GCC GCC GCG ATC CC 3′
S1: 5′ T ATG AAA AAA TAC CTA TTC CGa/g GCN GCN c/tTa/g TAc/t GGc/g ATC GCC GCC GCC ATC CTC GCC GCC GCG ATC CC 3′

[0252] The alignment of some of the mutants obtained is given below.

```
L1 mutants:
9L1-a    ATGAAGAAGTACCTTTTCAGCGCCGCC~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
9L1-e    ATGAAAAAATACTTTTTCCGCGCCGCC~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
9L1-d    ATGAAAAAATACTTTTTCCGCGCCGCC~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
9L1-f    ATGAAAAAATATCTCTTTAGCGCCGCCCTGTACGGCATCGCCGCCGCCATCCTCGCCGCC
919sp    ATGAAAAAATACCTATTCCGCGCCGCCCTGTACGGCATCGCCGCCGCCATCCTCGCCGCC

9L1a     MKKYLFSAA~~~~~~~~~~~
9L1e     MKKYFFRAA~~~~~~~~~~~
9L1d     MKKYFFRAA~~~~~~~~~~~
9L1f     MKKYLFSAALYGIAAAILAA
919sp    MKKYLFRAALYGIAAAILAA (i.e. native signal peptide)
```

```
S1 mutants:
9S1-e   ATGAAAAAATACCTATTC..................ATCGCCGCCGCCATCCTCGCCGCC
9S1-c   ATGAAAAAATACCTATTCCGAGCTGCCCAATACGGCATCGCCGCCGCCATCCTCGCCGCC
9S1-b   ATGAAAAAATACCTATTCCGGGCCGCCCAATACGGCATCGCCGCCGCCATCCTCGCCGCC
9S1-i   ATGAAAAAATACCTATTCCGGGCGGCTTTGTACGGGATCGCCGCCGCCATCCTCGCCGCC
919sp   ATGAAAAAATACCTATTCCGCGCCGCCCTGTACGGCATCGCCGCCGCCATCCTCGCCGCC

9S1e   MKKYLF......IAAAILAA
9S1c   MKKYLFRAAQYGIAAAILAA
9S1b   MKKYLFRAAQYGIAAAILAA
9S1i   MKKYLFRAALYGIAAAILAA
919sp  MKKYLFRAALYGIAAAILAA
```

[0253] As shown in the sequences alignments, most of the mutants analysed contain in-frame deletions which were unexpectedly produced by the host cells.

[0254] Selection of the mutants was performed by transforming *E. coli* BL21(DE3) cells with DNA prepared from a mixture of L1 and S1 mutated clones. Single transformants were screened for high PhoC activity by streaking them onto LB plates containing 100 μg/ml ampicillin, 50μg/ml methyl green, 1 mg/ml PDP (phenolphthaleindiphosphate). On this medium PhoC-producing cells become green (Figure 10).

[0255] A quantitative analysis of PhoC produced by these mutants was carried out in liquid medium using pNPP as a substrate for PhoC activity. The specific activities measured in cell extracts and supernatants of mutants grown in liquid medium for 0, 30, 90, 180 min. were:

CELL EXTRACTS

[0256]

	0	30	90	180
control	0,00	0,00	0,00	0,00
9phoC	1,11	1,11	3,33	4,44
9S1e	102,12	111,00	149,85	172,05
9L1a	206,46	111,00	94,35	83,25
9L1d	5,11	4,77	4,00	3,11
9L1f	27,75	94,35	82,14	36,63
9S1b	156,51	111,00	72,15	28,86
9S1c	72,15	33,30	21,09	14,43
9S1i	156,51	83,25	55,50	26,64
phoCwt	194,25	180,93	149,85	142,08

SUPERNATANTS

[0257]

	0	30	90	1801
control	0,00	0,00	0,00	0,00
9phoC	0,33	0,00	0,00	0,00
9S1e	0,11	0,22	0,44	0,89
9L1a	4,88	5,99	5,99	7,22
9L1d	0,11	0,11	0,11	0,11
9L1f	0,11	0,22	0,11	0,11
9S1b	1,44	1,44	1,44	1,67
9S1c	0,44	0,78	0,56	0,67
9S1i	0,22	0,44	0,22	0,78
phoCwt	34,41	43,29	87,69	177,60

[0258] Some of the mutants produce high amounts of PhoC and in particular, mutant 9L1a can secrete PhoC in the culture medium. This is noteworthy since the signal peptide sequence of this mutant is only 9 amino acids long. This is the shortest signal peptide described to date.

Example 21— C-terminal deletions of Maf-related proteins

[0259] MafB-related proteins include 730, ORF46 and ORF29.

[0260] The 730 protein from MC58 has the following sequence:

```
  1  VKPLRRLTNL LAACAVAAAA LIQPALAADL AQDPFITDNA QRQHYEPGGK
 51  YHLFGDPRGS VSDRTGKINV IQDYTHQMGN LLIQQANING TIGYHTRFSG
101  HGHEEHAPFD NHAADSASEE KGNVDEGFTV YRLNWEGHEH HPADAYDGPK
151  GGNYPKPTGA RDEYTYHVNG TARSIKLNPT DTRSIRQRIS DNYSNLGSNF
201  SDRADEANRK MFEHNAKLDR WGNSMEFING VAAGALNPFI SAGEALGIGD
251  ILYGTRYAID KAAMRNIAPL PAEGKFAVIG GLGSVAGFEK NTREAVDRWI
301  QENPNAAETV EAVFNVAAAA KVAKLAKAAK PGKAAVSGDF ADSYKKKLAL

351  SDSARQLYQN AKYREALDIH YEDLIRRKTD GSSKFINGRE IDAVTNDALI
401  QAKRTISAID KPKNFLNQKN RKQIKATIEA ANQQGKRAEF WFKYGVHSQV
451  KSYIESKGGI VKTGLGD*
```

[0261] The leader peptide is underlined.

[0262] 730 shows similar features to ORF46 (see example 8 above):

- as for Orf46, the conservation of the 730 sequence among MenB, MenA and gonococcus is high (>80%) only for the N-terminal portion. The C-terminus, from ~340, is highly divergent.
- its predicted secondary structure contains a hydrophobic segment spanning the central region of the molecule (aa. 227-247).
- expression of the full-length gene in *E. coli* gives very low yields of protein. Expression from tagged or untagged constructs where the signal peptide sequence has been omitted has a toxic effect on the host cells. In other words, the presence of the full-length mature protein in the cytoplasm is highly toxic for the host cell while its translocation to the periplasm (mediated by the signal peptide) has no detectable effect on cell viability. This "intracellular toxicity" of 730 is particularly high since clones for expression of the leaderless 730 can only be obtained at very low frequency using a *recA* genetic background (*E. coli* strains: HB101 for cloning; HMS174(DE3) for expression).

[0263] To overcome this toxicity, a similar approach was used for 730 as described in example 8 for ORF46. Four C-terminal truncated forms were obtained, each of which is well expressed. All were obtained from intracellular expression of His-tagged leaderless 730.

[0264] Form A consists of the N-terminal hydrophilic region of the mature protein (aa. 28-226). This was purified as a soluble His-tagged product, having a higher-than-expected MW.

[0265] Form B extends to the end of the region conserved between serogroups (aa. 28-340). This was purified as an insoluble His-tagged product.

[0266] The C-terminal truncated forms named C1 and C2 were obtained after screening for clones expressing high levels of 730-His clones in strain HMS174(DE3). Briefly, the pET21b plasmid containing the His-tagged sequence coding for the full-length mature 730 protein was used to transform the *recA* strain HMS 174(DE3). Transformants were obtained at low frequency which showed two phenotypes: large colonies and very small colonies. Several large and small colonies were analysed for expression of the 730-His clone. Only cells from large colonies over-expressed a protein recognised by anti-730A antibodies. However the protein over-expressed in different clones showed differences in molecular mass. Sequencing of two of the clones revealed that in both cases integration of an *E. coli* IS sequence had occurred within the sequence coding for the C terminal region of 730. The two integration events have produced in-frame fusion with 1 additional codon in the case of C1, and 12 additional codons in the case of C2 (Figure 11). The resulting "mutant" forms of 730 have the following sequences:

730-C1 (due to an IS1 insertion - figure 11A)

```
  1  MADLAQDPFI TDNAQRQHYE PGGKYHLFGD PRGSVSDRTG KINVIQDYTH
 51  QMGNLLIQQA NINGTIGYHT RFSGHGHEEH APFDNHAADS ASEEKGNVDE
101  GFTVYRLNWE GHEHHPADAY DGPKGGNYPK PTGARDEYTY HVNGTARSIK
151  LNPTDTRSIR QRISDNYSNL GSNFSDRADE ANRKMFEHNA KLDRWGNSME
201  FINGVAAGAL NPFISAGEAL GIGDILYGTR YAIDKAAMRN IAPLPAEGKF
251  AVIGGLGSVA GFEKNTREAV DRWIQENPNA AETVEAVFNV AAAAKVAKLA
301  KAAKPGKAAV SGDFADSYKK KLALSDSARQ LYQNAKYREA LDIHYEDLIR
351  RKTDGSSKFI NGREIDAVTN DALIQAR*
```

[0267] The additional amino acid produced by the insertion is underlined.

730-C2 (due to an IS5 insertion - Figure 11B)

```
  1  MADLAQDPFI TDNAQRQHYE PGGKYHLFGD PRGSVSDRTG KINVIQDYTH
 51  QMGNLLIQQA NINGTIGYHT RFSGHGHEEH APFDNHAADS ASEEKGNVDE
101  GFTVYRLNWE GHEHHPADAY DGPKGGNYPK PTGARDEYTY HVNGTARSIK
151  LNPTDTRSIR QRISDNYSNL GSNFSDRADE ANRKMFEHNA KLDRWGNSME
201  FINGVAAGAL NPFISAGEAL GIGDILYGTR YAIDKAAMRN IAPLPAEGKF
251  AVIGGLGSVA GFEKNTREAV DRWIQENPNA AETVEAVFNV AAAAKVAKLA
301  KAAKPGKAAV SGDFADSYKK KLALSDSARQ LYQNAKYREA LGKVRISGEI
351  LLG*
```

[0268] The additional amino acids produced by the insertion are underlined.

[0269] In conclusion, intracellular expression of the 730-C1 form gives very high level of protein and has no toxic effect on the host cells, whereas the presence of the native C-terminus is toxic. These data suggest that the "intracellular toxicity" of 730 is associated with the C-terminal 65 amino acids of the protein.

[0270] Equivalent truncation of ORF29 to the first 231 or 368 amino acids has been performed, using expression with or without the leader peptide (amino acids 1-26; deletion gives cytoplasmic expression) and with or without a His-tag.

Example 22 - domains in 961

[0271] As described in example 9 above, the GST-fusion of 961 was the best-expressed in *E.coli.* To improve expression, the protein was divided into domains (figure 12).

[0272] The domains of 961 were designed on the basis of YadA (an adhesin produced by *Yersinia* which has been demonstrated to be an adhesin localized on the bacterial surface that forms oligomers that generate surface projection [Hoiczyk et al. (2000) EMBO J 19:5989-99]) and are: leader peptide, head domain, coiled-coil region (stalk), and membrane anchor domain.

[0273] These domains were expressed with or without the leader peptide, and optionally fused either to C-terminal His-tag or to N-terminal GST. *E.coli* clones expressing different domains of 961 were analyzed by SDS-PAGE and

western blot for the production and localization of the expressed protein, from over-night (o/n) culture or after 3 hours induction with IPTG. The results were:

	Total lysate (Western Blot)	Periplasm (Western Blot)	Supernatant (Western Blot)	OMV SDS-PAGE
961 (o/n) 961 (IPTG)	- +/-	- -	- -	
961-L (o/n) 961-L (IPTG)	+ +	- -	- -	+ +
961c-L (o/n) 961 c-L (IPTG)	- +	- +	- +	
961Δ_1-L (o/n) 961Δ_1-L (IPTG)	- +	- -	- -	 +

[0274] The results show that in *E. coli:*

- 961-L is highly expressed and localized on the outer membrane. By western blot analysis two specific bands have been detected: one at ~45kDa (the predicted molecular weight) and one at ~180kDa, indicating that 961-L can form oligomers. Additionally, these aggregates are more expressed in the over-night culture (without IPTG induction). OMV preparations of this clone were used to immunize mice and serum was obtained. Using overnight culture (predominantly by oligomeric form) the serum was bactericidal; the IPTG-induced culture (predominantly monomeric) was not bactericidal.

- 961Δ_1-L (with a partial deletion in the anchor region) is highly expressed and localized on the outer membrane, but does not form oligomers;

- the 961c-L (without the anchor region) is produced in soluble form and exported in the supernatant.

[0275] Titres in ELISA and in the serum bactericidal assay using His-fusions were as follows:

	ELISA	Bactericidal
961a (aa 24-268)	24397	4096
961b (aa 269-405)	7763	64
961c-L	29770	8192
961c (2996)	30774	>65536
961c (MC58)	33437	16384
961d	26069	>65536

[0276] *E.coli* clones expressing different forms of 961 (961, 961-L, 961Δ_1-L and 961c-L) were used to investigate if the 961 is an adhesin (*c.f.* YadA). An adhesion assay was performed using (a) the human epithelial cells and (b) *E.coli* clones after either over-night culture or three hours IPTG induction. 961-L grown over-night (961Δ_1-L) and IPTG-induced 961c-L (the clones expressing protein on surface) adhere to human epithelial cells.

[0277] 961c was also used in hybrid proteins (see above). As 961 and its domain variants direct efficient expression, they are ideally suited as the N-terminal portion of a hybrid protein.

Example 23* — *further hybrids

[0278] Further hybrid proteins of the invention are shown below (see also Figure 14). These are advantageous when compared to the individual proteins:

ORF46.1-741

```
1     ATGTCAGATT TGGCAAACGA TTCTTTTATC CGGCAGGTTC TCGACCGTCA
51    GCATTTCGAA CCCGACGGGA AATACCACCT ATTCGGCAGC AGGGGGGAAC
101   TTGCCGAGCG CAGCGGCCAT ATCGGATTGG GAAAAATACA AAGCCATCAG
151   TTGGGCAACC TGATGATTCA ACAGGCGGCC ATTAAAGGAA ATATCGGCTA
201   CATTGTCCGC TTTTCCGATC ACGGGCACGA AGTCCATTCC CCCTTCGACA
251   ACCATGCCTC ACATTCCGAT TCTGATGAAG CCGGTAGTCC CGTTGACGGA
301   TTTAGCCTTT ACCGCATCCA TTGGGACGGA TACGAACACC ATCCCGCCGA
351   CGGCTATGAC GGGCCACAGG GCGGCGGCTA TCCCGCTCCC AAAGGCGCGA
401   GGGATATATA CAGCTACGAC ATAAAAGGCG TTGCCCAAAA TATCCGCCTC
451   AACCTGACCG ACAACCGCAG CACCGGACAA CGGCTTGCCG ACCGTTTCCA
501   CAATGCCGGT AGTATGCTGA CGCAAGGAGT AGGCGACGGA TTCAAACGCG
551   CCACCCGATA CAGCCCCGAG CTGGACAGAT CGGGCAATGC CGCCGAAGCC
601   TTCAACGGCA CTGCAGATAT CGTTAAAAAC ATCATCGGCG CGGCAGGAGA
651   AATTGTCGGC GCAGGCGATG CCGTGCAGGG CATAAGCGAA GGCTCAAACA
701   TTGCTGTCAT GCACGGCTTG GGTCTGCTTT CCACCGAAAA CAAGATGGCG
751   CGCATCAACG ATTTGGCAGA TATGGCGCAA CTCAAAGACT ATGCCGCAGC
801   AGCCATCCGC GATTGGGCAG TCCAAAACCC CAATGCCGCA CAAGGCATAG
851   AAGCCGTCAG CAATATCTTT ATGGCAGCCA TCCCCATCAA AGGGATTGGA
901   GCTGTTCGGG GAAAATACGG CTTGGGCGGC ATCACGGCAC ATCCTATCAA
951   GCGGTCGCAG ATGGGCGCGA TCGCATTGCC GAAAGGGAAA TCCGCCGTCA
1001  GCGACAATTT TGCCGATGCG GCATACGCCA AATACCCGTC CCCTTACCAT
1051  TCCCGAAATA TCCGTTCAAA CTTGGAGCAG CGTTACGGCA AAGAAAACAT
1101  CACCTCCTCA ACCGTGCCGC CGTCAAACGG CAAAAATGTC AAACTGGCAG
1151  ACCAACGCCA CCCGAAGACA GGCGTACCGT TTGACGGTAA AGGGTTTCCG
1201  AATTTTGAGA AGCACGTGAA ATATGATACG GGATCCGGAG GGGGTGGTGT
1251  CGCCGCCGAC ATCGGTGCGG GGCTTGCCGA TGCACTAACC GCACCGCTCG
1301  ACCATAAAGA CAAAGGTTTG CAGTCTTTGA CGCTGGATCA GTCCGTCAGG
1351  AAAAACGAGA AACTGAAGCT GGCGGCACAA GGTGCGGAAA AAACTTATGG
1401  AAACGGTGAC AGCCTCAATA CGGGCAAATT GAAGAACGAC AAGGTCAGCC
1451  GTTTCGACTT TATCCGCCAA ATCGAAGTGG ACGGGCAGCT CATTACCTTG
1501  GAGAGTGGAG AGTTCCAAGT ATACAAACAA AGCCATTCCG CCTTAACCGC
1551  CTTTCAGACC GAGCAAATAC AAGATTCGGA GCATTCCGGG AAGATGGTTG
1601  CGAAACGCCA GTTCAGAATC GGCGACATAG CGGGCGAACA TACATCTTTT

1651  GACAAGCTTC CCGAAGGCGG CAGGGCGACA TATCGCGGGA CGGCGTTCGG
1701  TTCAGACGAT GCCGGCGGAA AACTGACCTA CACCATAGAT TTCGCCGCCA
1751  AGCAGGGAAA CGGCAAAATC GAACATTTGA AATCGCCAGA ACTCAATGTC
1801  GACCTGGCCG CCGCCGATAT CAAGCCGGAT GGAAAACGCC ATGCCGTCAT
1851  CAGCGGTTCC GTCCTTTACA ACCAAGCCGA GAAAGGCAGT TACTCCCTCG
1901  GTATCTTTGG CGGAAAAGCC CAGGAAGTTG CCGGCAGCGC GGAAGTGAAA
1951  ACCGTAAACG GCATACGCCA TATCGGCCTT GCCGCCAAGC AACTCGAGCA
2001  CCACCACCAC CACCACTGA
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1     MSDLANDSFI RQVLDRQHFE PDGKYHLFGS RGELAERSGH IGLGKIQSHQ
51    LGNLMIQQAA IKGNIGYIVR FSDHGHEVHS PFDNHASHSD SDEAGSPVDG
101   FSLYRIHWDG YEHHPADGYD GPQGGGYPAP KGARDIYSYD IKGVAQNIRL
151   NLTDNRSTGQ RLADRFHNAG SMLTQGVGDG FKRATRYSPE LDRSGNAAEA
201   FNGTADIVKN IIGAAGEIVG AGDAVQGISE GSNIAVMHGL GLLSTENKMA
251   RINDLADMAQ LKDYAAAAIR DWAVQNPNAA QGIEAVSNIF MAAIPIKGIG
301   AVRGKYGLGG ITAHPIKRSQ MGAIALPKGK SAVSDNFADA AYAKYPSPYH
351   SRNIRSNLEQ RYGKENITSS TVPPSNGKNV KLADQRHPKT GVPFDGKGFP
401   NFEKHVKYDT GSGGGGVAAD IGAGLADALT APLDHKDKGL QSLTLDQSVR
451   KNEKLKLAAQ GAEKTYGNGD SLNTGKLKND KVSRFDFIRQ IEVDGQLITL
501   ESGEFQVYKQ SHSALTAFQT EQIQDSEHSG KMVAKRQFRI GDIAGEHTSF
551   DKLPEGGRAT YRGTAFGSDD AGGKLTYTID FAAKQGNGKI EHLKSPELNV
601   DLAAADIKPD GKRHAVISGS VLYNQAEKGS YSLGIFGGKA QEVAGSAEVK
651   TVNGIRHIGL AAKQLEHHHH HH*
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ORF46.1-961

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   1 ATGTCAGATT TGGCAAACGA TTCTTTTATC CGGCAGGTTC TCGACCGTCA
  51 GCATTTCGAA CCCGACGGGA AATACCACCT ATTCGGCAGC AGGGGGGAAC
 101 TTGCCGAGCG CAGCGGCCAT ATCGGATTGG GAAAAATACA AAGCCATCAG
 151 TTGGGCAACC TGATGATTCA ACAGGCGGCC ATTAAAGGAA ATATCGGCTA
 201 CATTGTCCGC TTTTCCGATC ACGGGCACGA AGTCCATTCC CCCTTCGACA
 251 ACCATGCCTC ACATTCCGAT TCTGATGAAG CCGGTAGTCC CGTTGACGGA
 301 TTTAGCCTTT ACCGCATCCA TTGGGACGGA TACGAACACC ATCCCGCCGA
 351 CGGCTATGAC GGGCCACAGG GCGGCGGCTA TCCCGCTCCC AAAGGCGCGA
 401 GGGATATATA CAGCTACGAC ATAAAAGGCG TTGCCCAAAA TATCCGCCTC
 451 AACCTGACCG ACAACCGCAG CACCGGACAA CGGCTTGCCG ACCGTTTCCA
 501 CAATGCCGGT AGTATGCTGA CGCAAGGAGT AGGCGACGGA TTCAAACGCG
 551 CCACCCGATA CAGCCCCGAG CTGGACAGAT CGGGCAATGC CGCCGAAGCC
 601 TTCAACGGCA CTGCAGATAT CGTTAAAAAC ATCATCGGCG CGGCAGGAGA
 651 AATTGTCGGC GCAGGCGATG CCGTGCAGGG CATAAGCGAA GGCTCAAACA
 701 TTGCTGTCAT GCACGGCTTG GGTCTGCTTT CCACCGAAAA CAAGATGGCG
 751 CGCATCAACG ATTTGGCAGA TATGGCGCAA CTCAAAGACT ATGCCGCAGC
 801 AGCCATCCGC GATTGGGCAG TCCAAAACCC CAATGCCGCA CAAGGCATAG
 851 AAGCCGTCAG CAATATCTTT ATGGCAGCCA TCCCCATCAA AGGGATTGGA
 901 GCTGTTCGGG GAAAATACGG CTTGGGCGGC ATCACGGCAC ATCCTATCAA
 951 GCGGTCGCAG ATGGGCGCGA TCGCATTGCC GAAAGGGAAA TCCGCCGTCA
1001 GCGACAATTT TGCCGATGCG GCATACGCCA AATACCCGTC CCCTTACCAT
1051 TCCCGAAATA TCCGTTCAAA CTTGGAGCAG CGTTACGGCA AAGAAAACAT
1101 CACCTCCTCA ACCGTGCCGC CGTCAAACGG CAAAAATGTC AAACTGGCAG
1151 ACCAACGCCA CCCGAAGACA GGCGTACCGT TTGACGGTAA AGGGTTTCCG
1201 AATTTTGAGA AGCACGTGAA ATATGATACG GGATCCGGAG GAGGAGGAGC
1251 CACAAACGAC GACGATGTTA AAAAAGCTGC CACTGTGGCC ATTGCTGCTG
1301 CCTACAACAA TGGCCAAGAA ATCAACGGTT TCAAAGCTGG AGAGACCATC
1351 TACGACATTG ATGAAGACGG CACAATTACC AAAAAAGACG CAACTGCAGC
1401 CGATGTTGAA GCCGACGACT TTAAAGGTCT GGGTCTGAAA AAAGTCGTGA
1451 CTAACCTGAC CAAAACCGTC AATGAAAACA AACAAAACGT CGATGCCAAA
1501 GTAAAAGCTG CAGAATCTGA AATAGAAAAG TTAACAACCA AGTTAGCAGA
1551 CACTGATGCC GCTTTAGCAG ATACTGATGC CGCTCTGGAT GCAACCACCA
1601 ACGCCTTGAA TAAATTGGGA GAAAATATAA CGACATTTGC TGAAGAGACT
1651 AAGACAAATA TCGTAAAAAT TGATGAAAAA TTAGAAGCCG TGGCTGATAC
1701 CGTCGACAAG CATGCCGAAG CATTCAACGA TATCGCCGAT TCATTGGATG
1751 AAACCAACAC TAAGGCAGAC GAAGCCGTCA AAACCGCCAA TGAAGCCAAA
1801 CAGACGGCCG AAGAAACCAA ACAAAACGTC GATGCCAAAG TAAAAGCTGC
1851 AGAAACTGCA GCAGGCAAAG CCGAAGCTGC CGCTGGCACA GCTAATACTG
1901 CAGCCGACAA GGCCGAAGCT GTCGCTGCAA AAGTTACCGA CATCAAAGCT
1951 GATATCGCTA CGAACAAAGA TAATATTGCT AAAAAAGCAA ACAGTGCCGA
2001 CGTGTACACC AGAGAAGAGT CTGACAGCAA ATTTGTCAGA ATTGATGGTC

2051 TGAACGCTAC TACCGAAAAA TTGGACACAC GCTTGGCTTC TGCTGAAAAA
2101 TCCATTGCCG ATCACGATAC TCGCCTGAAC GGTTTGGATA AAACAGTGTC
2151 AGACCTGCGC AAAGAAACCC GCCAAGGCCT TGCAGAACAA GCCGCGCTCT
2201 CCGGTCTGTT CCAACCTTAC AACGTGGGTC GGTTCAATGT AACGGCTGCA
2251 GTCGGCGGCT ACAAATCCGA ATCGGCAGTC GCCATCGGTA CCGGCTTCCG
2301 CTTTACCGAA AACTTTGCCG CCAAAGCAGG CGTGGCAGTC GGCACTTCGT
2351 CCGGTTCTTC CGCAGCCTAC CATGTCGGCG TCAATTACGA GTGGCTCGAG
2401 CACCACCACC ACCACCACTG A
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  1 MSDLANDSFI RQVLDRQHFE PDGKYHLFGS RGELAERSGH IGLGKIQSHQ
 51 LGNLMIQQAA IKGNIGYIVR FSDHGHEVHS PFDNHASHSD SDEAGSPVDG
101 FSLYRIHWDG YEHHPADGYD GPQGGGYPAP KGARDIYSYD IKGVAQNIRL
151 NLTDNRSTGQ RLADRFHNAG SMLTQGVGDG FKRATRYSPE LDRSGNAAEA
201 FNGTADIVKN IIGAAGEIVG AGDAVQGISE GSNIAVMHGL GLLSTENKMA
251 RINDLADMAQ LKDYAAAAIR DWAVQNPNAA QGIEAVSNIF MAAIPIKGIG
301 AVRGKYGLGG ITAHPIKRSQ MGAIALPKGK SAVSDNFADA AYAKYPSPYH
351 SRNIRSNLEQ RYGKENITSS TVPPSNGKNV KLADQRHPKT GVPFDGKGFP
401 NFEKHVKYDT GSGGGGATND DDVKKAATVA IAAAYNNGQE INGFKAGETI
451 YDIDEDGTIT KKDATAADVE ADDFKGLGLK KVVTNLTKTV NENKQNVDAK
501 VKAAESEIEK LTTKLADTDA ALADTDAALD ATTNALNKLG ENITTFAEET
551 KTNIVKIDEK LEAVADTVDK HAEAFNDIAD SLDETNTKAD EAVKTANEAK
601 QTAEETKQNV DAKVKAAETA AGKAEAAAGT ANTAADKAEA VAAKVTDIKA
651 DIATNKDNIA KKANSADVYT REESDSKFVR IDGLNATTEK LDTRLASAEK
701 SIADHDTRLN GLDKTVSDLR KETRQGLAEQ AALSGLFQPY NVGRFNVTAA
751 VGGYKSESAV AIGTGFRFTE NFAAKAGVAV GTSSGSSAAY HVGVNYEWLE
801 HHHHHH*
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ORF46.1-961c

```
   1 ATGTCAGATT TGGCAAACGA TTCTTTTATC CGGCAGGTTC TCGACCGTCA
  51 GCATTTCGAA CCCGACGGGA AATACCACCT ATTCGGCAGC AGGGGGGAAC
 101 TTGCCGAGCG CAGCGGCCAT ATCGGATTGG GAAAAATACA AAGCCATCAG
 151 TTGGGCAACC TGATGATTCA ACAGGCGGCC ATTAAAGGAA ATATCGGCTA
 201 CATTGTCCGC TTTTCCGATC ACGGGCACGA AGTCCATTCC CCCTTCGACA
 251 ACCATGCCTC ACATTCCGAT TCTGATGAAG CCGGTAGTCC CGTTGACGGA
 301 TTTAGCCTTT ACCGCATCCA TTGGGACGGA TACGAACACC ATCCCGCCGA
 351 CGGCTATGAC GGGCCACAGG GCGGCGGCTA TCCCGCTCCC AAAGGCGCGA
 401 GGGATATATA CAGCTACGAC ATAAAAGGCG TTGCCCAAAA TATCCGCCTC
 451 AACCTGACCG ACAACCGCAG CACCGGACAA CGGCTTGCCG ACCGTTTCCA
 501 CAATGCCGGT AGTATGCTGA CGCAAGGAGT AGGCGACGGA TTCAAACGCG
 551 CCACCCGATA CAGCCCCGAG CTGGACAGAT CGGGCAATGC CGCCGAAGCC
 601 TTCAACGGCA CTGCAGATAT CGTTAAAAAC ATCATCGGCG CGGCAGGAGA
 651 AATTGTCGGC GCAGGCGATG CCGTGCAGGG CATAAGCGAA GGCTCAAACA
 701 TTGCTGTCAT GCACGGCTTG GGTCTGCTTT CCACCGAAAA CAAGATGGCG
 751 CGCATCAACG ATTTGGCAGA TATGGCGCAA CTCAAAGACT ATGCCGCAGC
 801 AGCCATCCGC GATTGGGCAG TCCAAAACCC CAATGCCGCA CAAGGCATAG
 851 AAGCCGTCAG CAATATCTTT ATGGCAGCCA TCCCCATCAA AGGGATTGGA
 901 GCTGTTCGGG GAAAATACGG CTTGGGCGGC ATCACGGCAC ATCCTATCAA
 951 GCGGTCGCAG ATGGGCGCGA TCGCATTGCC GAAAGGGAAA TCCGCCGTCA
1001 GCGACAATTT TGCCGATGCG GCATACGCCA AATACCCGTC CCCTTACCAT
1051 TCCCGAAATA TCCGTTCAAA CTTGGAGCAG CGTTACGGCA AAGAAAACAT
1101 CACCTCCTCA ACCGTGCCGC CGTCAAACGG CAAAAATGTC AAACTGGCAG
1151 ACCAACGCCA CCCGAAGACA GGCGTACCGT TTGACGGTAA AGGGTTTCCG
1201 AATTTTGAGA AGCACGTGAA ATATGATACG GGATCCGGAG GAGGAGGAGC
1251 CACAAACGAC GACGATGTTA AAAAAGCTGC CACTGTGGCC ATTGCTGCTG
1301 CCTACAACAA TGGCCAAGAA ATCAACGGTT TCAAAGCTGG AGAGACCATC
1351 TACGACATTG ATGAAGACGG CACAATTACC AAAAAAGACG CAACTGCAGC
1401 CGATGTTGAA GCCGACGACT TTAAAGGTCT GGGTCTGAAA AAAGTCGTGA
1451 CTAACCTGAC CAAAACCGTC AATGAAAACA AACAAAACGT CGATGCCAAA
1501 GTAAAAGCTG CAGAATCTGA AATAGAAAAG TTAACAACCA AGTTAGCAGA
1551 CACTGATGCC GCTTTAGCAG ATACTGATGC CGCTCTGGAT GCAACCACCA
1601 ACGCCTTGAA TAAATTGGGA GAAAATATAA CGACATTTGC TGAAGAGACT
1651 AAGACAAATA TCGTAAAAAT TGATGAAAAA TTAGAAGCCG TGGCTGATAC
1701 CGTCGACAAG CATGCCGAAG CATTCAACGA TATCGCCGAT TCATTGGATG
1751 AAACCAACAC TAAGGCAGAC GAAGCCGTCA AAACCGCCAA TGAAGCCAAA
1801 CAGACGGCCG AAGAAACCAA ACAAAACGTC GATGCCAAAG TAAAAGCTGC
1851 AGAAACTGCA GCAGGCAAAG CCGAAGCTGC CGCTGGCACA GCTAATACTG
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1901   CAGCCGACAA GGCCGAAGCT GTCGCTGCAA AAGTTACCGA CATCAAAGCT
1951   GATATCGCTA CGAACAAAGA TAATATTGCT AAAAAAGCAA ACAGTGCCGA
2001   CGTGTACACC AGAGAAGAGT CTGACAGCAA ATTTGTCAGA ATTGATGGTC
2051   TGAACGCTAC TACCGAAAAA TTGGACACAC GCTTGGCTTC TGCTGAAAAA
2101   TCCATTGCCG ATCACGATAC TCGCCTGAAC GGTTTGGATA AAACAGTGTC
2151   AGACCTGCGC AAAGAAACCC GCCAAGGCCT TGCAGAACAA GCCGCGCTCT
2201   CCGGTCTGTT CCAACCTTAC AACGTGGGTC TCGAGCACCA CCACCACCAC
2251   CACTGA
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  1   MSDLANDSFI RQVLDRQHFE PDGKYHLFGS RGELAERSGH IGLGKIQSHQ
 51   LGNLMIQQAA IKGNIGYIVR FSDHGHEVHS PFDNHASHSD SDEAGSPVDG
101   FSLYRIHWDG YEHHPADGYD GPQGGGYPAP KGARDIYSYD IKGVAQNIRL
151   NLTDNRSTGQ RLADRFHNAG SMLTQGVGDG FKRATRYSPE LDRSGNAAEA
201   FNGTADIVKN IIGAAGEIVG AGDAVQGISE GSNIAVMHGL GLLSTENKMA
251   RINDLADMAQ LKDYAAAAIR DWAVQNPNAA QGIEAVSNIF MAAIPIKGIG
301   AVRGKYGLGG ITAHPIKRSQ MGAIALPKGK SAVSDNFADA AYAKYPSPYH
351   SRNIRSNLEQ RYGKENITSS TVPPSNGKNV KLADQRHPKT GVPFDGKGFP
401   NFEKHVKYDT GSGGGGATND DDVKKAATVA IAAAYNNGQE INGFKAGETI
451   YDIDEDGTIT KKDATAADVE ADDFKGLGLK KVVTNLTKTV NENKQNVDAK
501   VKAAESEIEK LTTKLADTDA ALADTDAALD ATTNALNKLG ENITTFAEET
551   KTNIVKIDEK LEAVADTVDK HAEAFNDIAD SLDETNTKAD EAVKTANEAK
601   QTAEETKQNV DAKVKAAETA AGKAEAAAGT ANTAADKAEA VAAKVTDIKA
651   DIATNKDNIA KKANSADVYT REESDSKFVR IDGLNATTEK LDTRLASAEK
701   SIADHDTRLN GLDKTVSDLR KETRQGLAEQ AALSGLFQPY NVGLEHHHHH
751   H*
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961-ORF46.1

```
   1 ATGGCCACAA ACGACGACGA TGTTAAAAAA GCTGCCACTG TGGCCATTGC
  51 TGCTGCCTAC AACAATGGCC AAGAAATCAA CGGTTTCAAA GCTGGAGAGA
 101 CCATCTACGA CATTGATGAA GACGGCACAA TTACCAAAAA AGACGCAACT
 151 GCAGCCGATG TTGAAGCCGA CGACTTTAAA GGTCTGGGTC TGAAAAAAGT
 201 CGTGACTAAC CTGACCAAAA CCGTCAATGA AAACAAACAA AACGTCGATG
 251 CCAAAGTAAA AGCTGCAGAA TCTGAAATAG AAAAGTTAAC AACCAAGTTA
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961c-ORF46.1

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2201  ATTTTGAGAA GCACGTGAAA TATGATACGC TCGAGCACCA CCACCACCAC
2251  CACTGA
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1    MATNDDDVKK AATVAIAAAY NNGQEINGFK AGETIYDIDE DGTITKKDAT
51   AADVEADDFK GLGLKKVVTN LTKTVNENKQ NVDAKVKAAE SEIEKLTTKL
101  ADTDAALADT DAALDATTNA LNKLGENITT FAEETKTNIV KIDEKLEAVA
151  DTVDKHAEAF NDIADSLDET NTKADEAVKT ANEAKQTAEE TKQNVDAKVK
201  AAETAAGKAE AAAGTANTAA DKAEAVAAKV TDIKADIATN KDNIAKKANS
251  ADVYTREESD SKFVRIDGLN ATTEKLDTRL ASAEKSIADH DTRLNGLDKT
301  VSDLRKETRQ GLAEQAALSG LFQPYNVGGS GGGGSDLAND SFIRQVLDRQ
351  HFEPDGKYHL FGSRGELAER SGHIGLGKIQ SHQLGNLMIQ QAAIKGNIGY
401  IVRFSDHGHE VHSPFDNHAS HSDSDEAGSP VDGFSLYRIH WDGYEHHPAD
451  GYDGPQGGGY PAPKGARDIY SYDIKGVAQN IRLNLTDNRS TGQRLADRFH
501  NAGSMLTQGV GDGFKRATRY SPELDRSGNA AEAFNGTADI VKNIIGAAGE
551  IVGAGDAVQG ISEGSNIAVM HGLGLLSTEN KMARINDLAD MAQLKDYAAA
601  AIRDWAVQNP NAAQGIEAVS NIFMAAIPIK GIGAVRGKYG LGGITAHPIK
651  RSQMGAIALP KGKSAVSDNF ADAAYAKYPS PYHSRNIRSN LEQRYGKENI
701  TSSTVPPSNG KNVKLADQRH PKTGVPFDGK GFPNFEKHVK YDTLEHHHHH

751  H*
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961c-741

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51   TGCTGCCTAC AACAATGGCC AAGAAATCAA CGGTTTCAAA GCTGGAGAGA
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151  GCAGCCGATG TTGAAGCCGA CGACTTTAAA GGTCTGGGTC TGAAAAAAGT
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451  GATACCGTCG ACAAGCATGC CGAAGCATTC AACGATATCG CCGATTCATT
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751  GCCGACGTGT ACACCAGAGA AGAGTCTGAC AGCAAATTTG TCAGAATTGA
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951  GCTCTCCGGT CTGTTCCAAC CTTACAACGT GGGTGGATCC GGAGGGGGTG
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1751 AGCACCACCA CCACCACCAC TGA
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  1  MATNDDDVKK AATVAIAAAY NNGQEINGFK AGETIYDIDE DGTITKKDAT
 51  AADVEADDFK GLGLKKVVTN LTKTVNENKQ NVDAKVKAAE SEIEKLTTKL
101  ADTDAALADT DAALDATTNA LNKLGENITT FAEETKTNIV KIDEKLEAVA
151  DTVDKHAEAF NDIADSLDET NTKADEAVKT ANEAKQTAEE TKQNVDAKVK
201  AAETAAGKAE AAAGTANTAA DKAEAVAAKV TDIKADIATN KDNIAKKANS
251  ADVYTREESD SKFVRIDGLN ATTEKLDTRL ASAEKSIADH DTRLNGLDKT
301  VSDLRKETRQ GLAEQAALSG LFQPYNVGGS GGGGVAADIG AGLADALTAP
351  LDHKDKGLQS LTLDQSVRKN EKLKLAAQGA EKTYGNGDSL NTGKLKNDKV
401  SRFDFIRQIE VDGQLITLES GEFQVYKQSH SALTAFQTEQ IQDSEHSGKM
451  VAKRQFRIGD IAGEHTSFDK LPEGGRATYR GTAFGSDDAG GKLTYTIDFA
501  AKQGNGKIEH LKSPELNVDL AAADIKPDGK RHAVISGSVL YNQAEKGSYS
551  LGIFGGKAQE VAGSAEVKTV NGIRHIGLAA KQLEHHHHHH *
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961c-983

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251  CCAAAGTAAA AGCTGCAGAA TCTGAAATAG AAAAGTTAAC AACCAAGTTA
301  GCAGACACTG ATGCCGCTTT AGCAGATACT GATGCCGCTC TGGATGCAAC
351  CACCAACGCC TTGAATAAAT TGGGAGAAAA TATAACGACA TTTGCTGAAG
401  AGACTAAGAC AAATATCGTA AAAATTGATG AAAAATTAGA AGCCGTGGCT
451  GATACCGTCG ACAAGCATGC CGAAGCATTC AACGATATCG CCGATTCATT
501  GGATGAAACC AACACTAAGG CAGACGAAGC CGTCAAAACC GCCAATGAAG
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1151  TTGCGGTTAC AGACAGGGAT GCCAAAATCA ATGCCCCCCC CCCGAATCTG
1201  CATACCGGAG ACTTTCCAAA CCCAAATGAC GCATACAAGA ATTTGATCAA
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2101  TGGTGCCTGT CGGCACCCTA TGAAGCAAGC GTCCGTTTCA CCCGTACAAA
2151  CCCGATTCAA ATTGCCGGAA CATCCTTTTC CGCACCCATC GTAACCGGCA
2201  CGGCGGCTCT GCTGCTGCAG AAATACCCGT GGATGAGCAA CGACAACCTG
2251  CGTACCACGT TGCTGACGAC GGCTCAGGAC ATCGGTGCAG TCGGCGTGGA
2301  CAGCAAGTTC GGCTGGGGAC TGCTGGATGC GGGTAAGGCC ATGAACGGAC
2351  CCGCGTCCTT TCCGTTCGGC GACTTTACCG CCGATACGAA AGGTACATCC
2401  GATATTGCCT ACTCCTTCCG TAACGACATT TCAGGCACGG GCGGCCTGAT
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2501  GCAAAACCAT TATCGAAGGC GGTTCGCTGG TGTTGTACGG CAACAACAAA
2551  TCGGATATGC GCGTCGAAAC CAAAGGTGCG CTGATTTATA ACGGGGCGGC
2601  ATCCGGCGGC AGCCTGAACA GCGACGGCAT TGTCTATCTG GCAGATACCG
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3701  GCGGTGTCAA CGTTCCGTTT GCCGCAACGG GAGATTTGAC GGTCGAAGGC
3751  GGTCTGCGCT ACGACCTGCT CAAACAGGAT GCATTCGCCG AAAAAGGCAG
3801  TGCTTTGGGC TGGAGCGGCA ACAGCCTCAC TGAAGGCACG CTGGTCGGAC
3851  TCGCGGGTCT GAAGCTGTCG CAACCCTTGA GCGATAAAGC CGTCCTGTTT
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3901  GCAACGGCGG GCGTGGAACG CGACCTGAAC GGACGCGACT ACACGGTAAC
3951  GGGCGGCTTT ACCGGCGCGA CTGCAGCAAC CGGCAAGACG GGGGCACGCA
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4051  GGCAACGGCT GGAACGGCTT GGCACGTTAC AGCTACGCCG GTTCCAAACA
4101  GTACGGCAAC CACAGCGGAC GAGTCGGCGT AGGCTACCGG TTCCTCGAGC
4151  ACCACCACCA CCACCACTGA
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   1  MATNDDDVKK AATVAIAAAY NNGQEINGFK AGETIYDIDE DGTITKKDAT
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 101  ADTDAALADT DAALDATTNA LNKLGENITT FAEETKTNIV KIDEKLEAVA
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 251  ADVYTREESD SKFVRIDGLN ATTEKLDTRL ASAEKSIADH DTRLNGLDKT
 301  VSDLRKETRQ GLAEQAALSG LFQPYNVGGS GGGGTSAPDF NAGGTGIGSN
 351  SRATTAKSAA VSYAGIKNEM CKDRSMLCAG RDDVAVTDRD AKINAPPPNL
 401  HTGDFPNPND AYKNLINLKP AIEAGYTGRG VEVGIVDTGE SVGSISFPEL
 451  YGRKEHGYNE NYKNYTAYMR KEAPEDGGGK DIEASFDDEA VIETEAKPTD
 501  IRHVKEIGHI DLVSHIIGGR SVDGRPAGGI APDATLHIMN TNDETKNEMM
 551  VAAIRNAWVK LGERGVRIVN NSFGTTSRAG TADLFQIANS EEQYRQALLD
 601  YSGGDKTDEG IRLMQQSDYG NLSYHIRNKN MLFIFSTGND AQAQPNTYAL
 651  LPFYEKDAQK GIITVAGVDR SGEKFKREMY GEPGTEPLEY GSNHCGITAM
 701  WCLSAPYEAS VRFTRTNPIQ IAGTSFSAPI VTGTAALLLQ KYPWMSNDNL
 751  RTTLLTTAQD IGAVGVDSKF GWGLLDAGKA MNGPASFPFG DFTADTKGTS
 801  DIAYSFRNDI SGTGGLIKKG GSQLQLHGNN TYTGKTIIEG GSLVLYGNNK
 851  SDMRVETKGA LIYNGAASGG SLNSDGIVYL ADTDQSGANE TVHIKGSLQL
 901  DGKGTLYTRL GKLLKVDGTA IIGGKLYMSA RGKGAGYLNS TGRRVPFLSA
 951  AKIGQDYSFF TNIETDGGLL ASLDSVEKTA GSEGDTLSYY VRRGNAARTA
1001  SAAAHSAPAG LKHAVEQGGS NLENLMVELD ASESSATPET VETAAADRTD
1051  MPGIRPYGAT FRAAAAVQHA NAADGVRIFN SLAATVYADS TAAHADMQGR
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1151  TGENTTAAAT LGMGRSTWSE NSANAKTDSI SLFAGIRHDA GDIGYLKGLF
1201  SYGRYKNSIS RSTGADEHAE GSVNGTLMQL GALGGVNVPF AATGDLTVEG
1251  GLRYDLLKQD AFAEKGSALG WSGNSLTEGT LVGLAGLKLS QPLSDKAVLF
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961cL-ORF46.1

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2301 CGAG
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151  TTFAEETKTN IVKIDEKLEA VADTVDKHAE AFNDIADSLD ETNTKADEAV
201  KTANEAKQTA EETKQNVDAK VKAAETAAGK AEAAAGTANT AADKAEAVAA
251  KVTDIKADIA TNKDNIAKKA NSADVYTREE SDSKFVRIDG LNATTEKLDT
301  RLASAEKSIA DHDTRLNGLD KTVSDLRKET RQGLAEQAAL SGLFQPYNVG
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401  IQSHQLGNLM IQQAAIKGNI GYIVRFSDHG HEVHSPFDNH ASHSDSDEAG
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501  QNIRLNLTDN RSTGQRLADR FHNAGSMLTQ GVGDGFKRAT RYSPELDRSG
551  NAAEAFNGTA DIVKNIIGAA GEIVGAGDAV QGISEGSNIA VMHGLGLLST
601  ENKMARINDL ADMAQLKDYA AAAIRDWAVQ NPNAAQGIEA VSNIFMAAIP
651  IKGIGAVRGK YGLGGITAHP IKRSQMGAIA LPKGKSAVSD NFADAAYAKY
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751  GKGFPNFEKH VKYDT*
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<u>961cL-741</u>

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1151  CGCTGGATCA GTCCGTCAGG AAAAACGAGA AACTGAAGCT GGCGGCACAA
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1251  GAAGAACGAC AAGGTCAGCC GTTTCGACTT TATCCGCCAA ATCGAAGTGG
1301  ACGGGCAGCT CATTACCTTG GAGAGTGGAG AGTTCCAAGT ATACAAACAA
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1401  GCATTCCGGG AAGATGGTTG CGAAACGCCA GTTCAGAATC GGCGACATAG
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1451  CGGGCGAACA TACATCTTTT GACAAGCTTC CCGAAGGCGG CAGGGCGACA
1501  TATCGCGGGA CGGCGTTCGG TTCAGACGAT GCCGGCGGAA AACTGACCTA
1551  CACCATAGAT TTCGCCGCCA AGCAGGGAAA CGGCAAAATC GAACATTTGA
1601  AATCGCCAGA ACTCAATGTC GACCTGGCCG CCGCCGATAT CAAGCCGGAT
1651  GGAAAACGCC ATGCCGTCAT CAGCGGTTCC GTCCTTTACA ACCAAGCCGA
1701  GAAAGGCAGT TACTCCCTCG GTATCTTTGG CGGAAAAGCC CAGGAAGTTG
1751  CCGGCAGCGC GGAAGTGAAA ACCGTAAACG GCATACGCCA TATCGGCCTT
1801  GCCGCCAAGC AACTCGAGCA CCACCACCAC CACCACTGA
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  1   MKHFPSKVLT TAILATFCSG ALAATNDDDV KKAATVAIAA AYNNGQEING
 51   FKAGETIYDI DEDGTITKKD ATAADVEADD FKGLGLKKVV TNLTKTVNEN
101   KQNVDAKVKA AESEIEKLTT KLADTDAALA DTDAALDATT NALNKLGENI
151   TTFAEETKTN IVKIDEKLEA VADTVDKHAE AFNDIADSLD ETNTKADEAV
201   KTANEAKQTA EETKQNVDAK VKAAETAAGK AEAAAGTANT AADKAEAVAA
251   KVTDIKADIA TNKDNIAKKA NSADVYTREE SDSKFVRIDG LNATTEKLDT
301   RLASAEKSIA DHDTRLNGLD KTVSDLRKET RQGLAEQAAL SGLFQPYNVG
351   GSGGGGVAAD IGAGLADALT APLDHKDKGL QSLTLDQSVR KNEKLKLAAQ
401   GAEKTYGNGD SLNTGKLKND KVSRFDFIRQ IEVDGQLITL ESGEFQVYKQ
451   SHSALTAFQT EQIQDSEHSG KMVAKRQFRI GDIAGEHTSF DKLPEGGRAT
501   YRGTAFGSDD AGGKLTYTID FAAKQGNGKI EHLKSPELNV DLAAADIKPD
551   GKRHAVISGS VLYNQAEKGS YSLGIFGGKA QEVAGSAEVK TVNGIRHIGL
601   AAKQLEHHHH HH*
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961cL-983

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   1   ATGAAACACT TTCCATCCAA AGTACTGACC ACAGCCATCC TTGCCACTTT
  51   CTGTAGCGGC GCACTGGCAG CCACAAACGA CGACGATGTT AAAAAAGCTG
 101   CCACTGTGGC CATTGCTGCT GCCTACAACA ATGGCCAAGA AATCAACGGT
 151   TTCAAAGCTG GAGAGACCAT CTACGACATT GATGAAGACG GCACAATTAC
 201   CAAAAAAGAC GCAACTGCAG CCGATGTTGA AGCCGACGAC TTTAAAGGTC
 251   TGGGTCTGAA AAAAGTCGTG ACTAACCTGA CCAAAACCGT CAATGAAAAC
 301   AAACAAAACG TCGATGCCAA AGTAAAAGCT GCAGAATCTG AAATAGAAAA
 351   GTTAACAACC AAGTTAGCAG ACACTGATGC CGCTTTAGCA GATACTGATG
 401   CCGCTCTGGA TGCAACCACC AACGCCTTGA ATAAATTGGG AGAAAATATA
 451   ACGACATTTG CTGAAGAGAC TAAGACAAAT ATCGTAAAAA TTGATGAAAA
 501   ATTAGAAGCC GTGGCTGATA CCGTCGACAA GCATGCCGAA GCATTCAACG
 551   ATATCGCCGA TTCATTGGAT GAAACCAACA CTAAGGCAGA CGAAGCCGTC
 601   AAAACCGCCA ATGAAGCCAA ACAGACGGCC GAAGAAACCA AACAAAACGT
 651   CGATGCCAAA GTAAAAGCTG CAGAAACTGC AGCAGGCAAA GCCGAAGCTG
 701   CCGCTGGCAC AGCTAATACT GCAGCCGACA AGGCCGAAGC TGTCGCTGCA
 751   AAAGTTACCG ACATCAAAGC TGATATCGCT ACGAACAAAG ATAATATTGC
 801   TAAAAAAGCA AACAGTGCCG ACGTGTACAC CAGAGAAGAG TCTGACAGCA
 851   AATTTGTCAG AATTGATGGT CTGAACGCTA CTACCGAAAA ATTGGACACA
 901   CGCTTGGCTT CTGCTGAAAA ATCCATTGCC GATCACGATA CTCGCCTGAA
 951   CGGTTTGGAT AAAACAGTGT CAGACCTGCG CAAAGAAACC CGCCAAGGCC
1001   TTGCAGAACA AGCCGCGCTC TCCGGTCTGT TCCAACCTTA CAACGTGGGT
1051   GGATCCGGCG GAGGCGGCAC TTCTGCGCCC GACTTCAATG CAGGCGGTAC
1101   CGGTATCGGC AGCAACAGCA GAGCAACAAC AGCGAAATCA GCAGCAGTAT
1151   CTTACGCCGG TATCAAGAAC GAAATGTGCA AAGACAGAAG CATGCTCTGT
1201   GCCGGTCGGG ATGACGTTGC GGTTACAGAC AGGGATGCCA AAATCAATGC
1251   CCCCCCCCCG AATCTGCATA CCGGAGACTT TCCAAACCCA AATGACGCAT
1301   ACAAGAATTT GATCAACCTC AAACCTGCAA TTGAAGCAGG CTATACAGGA
1351   CGCGGGGTAG AGGTAGGTAT CGTCGACACA GGCGAATCCG TCGGCAGCAT
1401   ATCCTTTCCC GAACTGTATG GCAGAAAAGA ACACGGCTAT AACGAAAATT
1451   ACAAAAAACTA TACGGCGTAT ATGCGGAAGG AAGCGCCTGA AGACGGAGGC
1501   GGTAAAGACA TTGAAGCTTC TTTCGACGAT GAGGCCGTTA TAGAGACTGA
1551   AGCAAAGCCG ACGGATATCC GCCACGTAAA AGAAATCGGA CACATCGATT
1601   TGGTCTCCCA TATTATTGGC GGGCGTTCCG TGGACGGCAG ACCTGCAGGC
1651   GGTATTGCGC CCGATGCGAC GCTACACATA ATGAATACGA ATGATGAAAC
1701   CAAGAACGAA ATGATGGTTG CAGCCATCCG CAATGCATGG GTCAAGCTGG
1751   GCGAACGTGG CGTGCGCATC GTCAATAACA GTTTTGGAAC AACATCGAGG
1801   GCAGGCACTG CCGACCTTTT CCAAATAGCC AATTCGGAGG AGCAGTACCG
1851   CCAAGCGTTG CTCGACTATT CCGGCGGTGA TAAAACAGAC GAGGGTATCC
1901   GCCTGATGCA ACAGAGCGAT TACGGCAACC TGTCCTACCA CATCCGTAAT
1951   AAAAACATGC TTTTCATCTT TTCGACAGGC AATGACGCAC AAGCTCAGCC
2001   CAACACATAT GCCCTATTGC CATTTTATGA AAAAGACGCT CAAAAAGGCA
2051   TTATCACAGT CGCAGGCGTA GACCGCAGTG GAGAAAAGTT CAAACGGGAA
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2101   ATGTATGGAG AACCGGGTAC AGAACCGCTT GAGTATGGCT CCAACCATTG
2151   CGGAATTACT GCCATGTGGT GCCTGTCGGC ACCCTATGAA GCAAGCGTCC
2201   GTTTCACCCG TACAAACCCG ATTCAAATTG CCGGAACATC CTTTTCCGCA
2251   CCCATCGTAA CCGGCACGGC GGCTCTGCTG CTGCAGAAAT ACCCGTGGAT
2301   GAGCAACGAC AACCTGCGTA CCACGTTGCT GACGACGGCT CAGGACATCG
2351   GTGCAGTCGG CGTGGACAGC AAGTTCGGCT GGGGACTGCT GGATGCGGGT
2401   AAGGCCATGA ACGGACCCGC GTCCTTTCCG TTCGGCGACT TTACCGCCGA
2451   TACGAAAGGT ACATCCGATA TTGCCTACTC CTTCCGTAAC GACATTTCAG
2501   GCACGGGCGG CCTGATCAAA AAAGGCGGCA GCCAACTGCA ACTGCACGGC
2551   AACAACACCT ATACGGGCAA AACCATTATC GAAGGCGGTT CGCTGGTGTT
2601   GTACGGCAAC AACAAATCGG ATATGCGCGT CGAAACCAAA GGTGCGCTGA
2651   TTTATAACGG GGCGGCATCC GGCGGCAGCC TGAACAGCGA CGGCATTGTC
2701   TATCTGGCAG ATACCGACCA ATCCGGCGCA AACGAAACCG TACACATCAA
2751   AGGCAGTCTG CAGCTGGACG GCAAAGGTAC GCTGTACACA CGTTTGGGCA
2801   AACTGCTGAA AGTGGACGGT ACGGCGATTA TCGGCGGCAA GCTGTACATG
2851   TCGGCACGCG GCAAGGGGGC AGGCTATCTC AACAGTACCG GACGACGTGT
2901   TCCCTTCCTG AGTGCCGCCA AAATCGGGCA GGATTATTCT TTCTTCACAA
2951   ACATCGAAAC CGACGGCGGC CTGCTGGCTT CCCTCGACAG CGTCGAAAAA
3001   ACAGCGGGCA GTGAAGGCGA CACGCTGTCC TATTATGTCC GTCGCGGCAA
3051   TGCGGCACGG ACTGCTTCGG CAGCGGCACA TTCCGCGCCC GCCGGTCTGA
3101   AACACGCCGT AGAACAGGGC GGCAGCAATC TGGAAAACCT GATGGTCGAA
3151   CTGGATGCCT CCGAATCATC CGCAACACCC GAGACGGTTG AAACTGCGGC
3201   AGCCGACCGC ACAGATATGC CGGGCATCCG CCCCTACGGC GCAACTTTCC
3251   GCGCAGCGGC AGCCGTACAG CATGCGAATG CCGCCGACGG TGTACGCATC
3301   TTCAACAGTC TCGCCGCTAC CGTCTATGCC GACAGTACCG CCGCCCATGC
3351   CGATATGCAG GGACGCCGCC TGAAAGCCGT ATCGGACGGG TTGGACCACA
3401   ACGGCACGGG TCTGCGCGTC ATCGCGCAAA CCCAACAGGA CGGTGGAACG
3451   TGGGAACAGG GCGGTGTTGA AGGCAAAATG CGCGGCAGTA CCCAAACCGT
3501   CGGCATTGCC GCGAAAACCG GCGAAAATAC GACAGCAGCC GCCACACTGG
3551   GCATGGGACG CAGCACATGG AGCGAAAACA GTGCAAATGC AAAAACCGAC
3601   AGCATTAGTC TGTTTGCAGG CATACGGCAC GATGCGGGCG ATATCGGCTA
3651   TCTCAAAGGC CTGTTCTCCT ACGGACGCTA CAAAAACAGC ATCAGCCGCA
3701   GCACCGGTGC GGACGAACAT GCGGAAGGCA GCGTCAACGG CACGCTGATG
3751   CAGCTGGGCG CACTGGGCGG TGTCAACGTT CCGTTTGCCG CAACGGGAGA
3801   TTTGACGGTC GAAGGCGGTC TGCGCTACGA CCTGCTCAAA CAGGATGCAT
3851   TCGCCGAAAA AGGCAGTGCT TTGGGCTGGA GCGGCAACAG CCTCACTGAA
3901   GGCACGCTGG TCGGACTCGC GGGTCTGAAG CTGTCGCAAC CCTTGAGCGA
3951   TAAAGCCGTC CTGTTTGCAA CGGCGGGCGT GGAACGCGAC CTGAACGGAC
4001   GCGACTACAC GGTAACGGGC GGCTTTACCG GCGCGACTGC AGCAACCGGC
4051   AAGACGGGGG CACGCAATAT GCCGCACACC CGTCTGGTTG CCGGCCTGGG
4101   CGCGGATGTC GAATTCGGCA ACGGCTGGAA CGGCTTGGCA CGTTACAGCT
4151   ACGCCGGTTC CAAACAGTAC GGCAACCACA GCGGACGAGT CGGCGTAGGC
4201   TACCGGTTCT GACTCGAG
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   1  MKHFPSKVLT TAILATFCSG ALAATNDDDV KKAATVAIAA AYNNGQEING
  51  FKAGETIYDI DEDGTITKKD ATAADVEADD FKGLGLKKVV TNLTKTVNEN
 101  KQNVDAKVKA AESEIEKLTT KLADTDAALA DTDAALDATT NALNKLGENI
 151  TTFAEETKTN IVKIDEKLEA VADTVDKHAE AFNDIADSLD ETNTKADEAV
 201  KTANEAKQTA EETKQNVDAK VKAAETAAGK AEAAAGTANT AADKAEAVAA
 251  KVTDIKADIA TNKDNIAKKA NSADVYTREE SDSKFVRIDG LNATTEKLDT
 301  RLASAEKSIA DHDTRLNGLD KTVSDLRKET RQGLAEQAAL SGLFQPYNVG
 351  GSGGGGTSAP DFNAGGTGIG SNSRATTAKS AAVSYAGIKN EMCKDRSMLC
 401  AGRDDVAVTD RDAKINAPPP NLHTGDFPNP NDAYKNLINL KPAIEAGYTG
 451  RGVEVGIVDT GESVGSISFP ELYGRKEHGY NENYKNYTAY MRKEAPEDGG
 501  GKDIEASFDD EAVIETEAKP TDIRHVKEIG HIDLVSHIIG GRSVDGRPAG
 551  GIAPDATLHI MNTNDETKNE MMVAAIRNAW VKLGERGVRI VNNSFGTTSR
 601  AGTADLFQIA NSEEQYRQAL LDYSGGDKTD EGIRLMQQSD YGNLSYHIRN
 651  KNMLFIFSTG NDAQAQPNTY ALLPFYEKDA QKGIITVAGV DRSGEKFKRE
 701  MYGEPGTEPL EYGSNHCGIT AMWCLSAPYE ASVRFTRTNP IQIAGTSFSA
 751  PIVTGTAALL LQKYPWMSND NLRTTLLTTA QDIGAVGVDS KFGWGLLDAG
 801  KAMNGPASFP FGDFTADTKG TSDIAYSFRN DISGTGGLIK KGGSQLQLHG
 851  NNTYTGKTII EGGSLVLYGN NKSDMRVETK GALIYNGAAS GGSLNSDGIV
 901  YLADTDQSGA NETVHIKGSL QLDGKGTLYT RLGKLLKVDG TAIIGGKLYM
 951  SARGKGAGYL NSTGRRVPFL SAAKIGQDYS FFTNIETDGG LLASLDSVEK
1001  TAGSEGDTLS YYVRRGNAAR TASAAAHSAP AGLKHAVEQG GSNLENLMVE
1051  LDASESSATP ETVETAAADR TDMPGIRPYG ATFRAAAAVQ HANAADGVRI
1101  FNSLAATVYA DSTAAHADMQ GRRLKAVSDG LDHNGTGLRV IAQTQQDGGT

1151  WEQGGVEGKM RGSTQTVGIA AKTGENTTAA ATLGMGRSTW SENSANAKTD
1201  SISLFAGIRH DAGDIGYLKG LFSYGRYKNS ISRSTGADEH AEGSVNGTLM
1251  QLGALGGVNV PFAATGDLTV EGGLRYDLLK QDAFAEKGSA LGWSGNSLTE
1301  GTLVGLAGLK LSQPLSDKAV LFATAGVERD LNGRDYTVTG GFTGATAATG
1351  KTGARNMPHT RLVAGLGADV EFGNGWNGLA RYSYAGSKQY GNHSGRVGVG
1401  YRF*
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[0279] It will be understood that the invention has been described by way of example only and modifications may be made whilst remaining within the scope and spirit of the invention. For instance, the use of proteins from other strains is envisaged [*e.g.* see WO00/66741 for polymorphic sequences for ORF4, ORF40, ORF46, 225, 235, 287, 519, 726, 919 and 953].

EXPERIMENTAL DETAILS

FPLC protein purification

[0280] The following table summarises the FPLC protein purification that was used:

Protein	PI	Column	Buffer	pH	Protocol
$121.1^{untagged}$	6.23	Mono Q	Tris	8.0	A
$128.1^{untagged}$	5.04	Mono Q	Bis-Tris propane	6.5	A
406.1L	7.75	Mono Q	Diethanolamine	9.0	B
576.1L	5.63	Mono Q	Tris	7.5	B
$593^{untagged}$	8.79	Mono S	Hepes	7.4	A
$726^{untagged}$	4.95	Hi-trap S	Bis-Tris	6.0	A
$919^{untagged}$	10.5(-leader)	Mono S	Bicine	8.5	C
919Lorf4	10.4(-leader)	Mono S	Tris	8.0	B
920L	6.92(-leader)	Mono Q	Diethanolamine	8.5	A
953L	7.56(-leader)	Mono S	MES	6.6	D

(continued)

Protein	PI	Column	Buffer	pH	Protocol
$982^{untagged}$	4.73	Mono Q	Bis-Tris propane	6.5	A
919-287	6.58	Hi-trap Q	Tris	8.0	A
953-287	4.92	Mono Q	Bis-Tris propane	6.2	A

[0281] Buffer solutions included 20-120 mM NaCl, 5.0 mg/ml CHAPS and 10% v/v glycerol. The dialysate was centrifuged at 13000g for 20 min and applied to either a mono Q or mono S FPLC ion-exchange resin. Buffer and ion exchange resins were chosen according to the pl of the protein of interest and the recommendations of the FPLC protocol manual [Pharmacia: *FPLC Ion Exchange and Chromatofocussing; Principles and Methods.* Pharmacia Publication]. Proteins were eluted using a step-wise NaCl gradient. Purification was analysed by SDS-PAGE and protein concentration determined by the Bradford method.

[0282] The letter in the 'protocol' column refers to the following:

[0283] **FPLC-A:** Clones 121.1, 128.1, 593, 726, 982, periplasmic protein 920L and hybrid proteins 919-287, 953-287 were purified from the soluble fraction of *E.coli* obtained after disruption of the cells. Single colonies harbouring the plasmid of interest were grown overnight at 37°C in 20 ml of LB/Amp (100 μg/ml) liquid culture. Bacteria were diluted 1:30 in 1.0 L of fresh medium and grown at either 30°C or 37°C until the OD_{550} reached 0.6-08. Expression of recombinant protein was induced with IPTG at a final concentration of 1.0 mM. After incubation for 3 hours, bacteria were harvested by centrifugation at 8000g for 15 minutes at 4°C. When necessary cells were stored at -20°C. All subsequent procedures were performed on ice or at 4°C. For cytosolic proteins (121.1, 128.1, 593, 726 and 982) and periplasmic protein 920L, bacteria were resuspended in 25 ml of PBS containing complete protease inhibitor (Boehringer-Mannheim). Cells were lysed by by sonication using a Branson Sonifier 450. Disrupted cells were centrifuged at 8000g for 30 min to sediment unbroken cells and inclusion bodies and the supernatant taken to 35% v/v saturation by the addition of 3.9 M $(NH_4)_2SO_4$. The precipitate was sedimented at 8000g for 30 minutes. The supernatant was taken to 70% v/v saturation by the addition of 3.9 M $(NH_4)_2SO_4$ and the precipitate collected as above. Pellets containing the protein of interest were identified by SDS-PAGE and dialysed against the appropriate ion-exchange buffer (see below) for 6 hours or overnight. The periplasmic fraction from *E.coli* expressing 953L was prepared according to the protocol of Evans et. al. [Infect.Immun. (1974), 10:1010-1017] and dialysed against the appropriate ion-exchange buffer. Buffer and ion exchange resin were chosen according to the pl of the protein of interest and the recommendations of the FPLC protocol manual (Pharmacia). Buffer solutions included 20 mM NaCl, and 10% (v/v) glycerol. The dialysate was centrifuged at 13000g for 20 min and applied to either a mono Q or mono S FPLC ion-exchange resin. Buffer and ion exchange resin were chosen according to the pl of the protein of interest and the recommendations of the FPLC protocol manual (Pharmacia). Proteins were eluted from the ion-exchange resin using either step-wise or continuous NaCl gradients. Purification was analysed by SDS-PAGE and protein concentration determined by Bradford method. Cleavage of the leader peptide of periplasmic proteins was demonstrated by sequencing the NH_2-terminus (see below).

[0284] **FPLC-B:** These proteins were purified from the membrane fraction of *E.coli.* Single colonies harbouring the plasmid of interest were grown overnight at 37°C in 20 ml of LB/Amp (100 μg/ml) liquid culture. Bacteria were diluted 1:30 in 1.0 L of fresh medium. Clones 406.1L and 919LOrf4 were grown at 30°C and Orf25L and 576.1L at 37°C until the OD_{550} reached 0.6-0.8. In the case of 919LOrf4, growth at 30°C was essential since expression of recombinant protein at 37°C resulted in lysis of the cells. Expression of recombinant protein was induced with IPTG at a final concentration of 1.0 mM. After incubation for 3 hours, bacteria were harvested by centrifugation at 8000g for 15 minutes at 4°C. When necessary cells were stored at -20 °C. All subsequent procedures were performed at 4°C. Bacteria were resuspended in 25 ml of PBS containing complete protease inhibitor (Boehringer-Mannheim) and lysed by osmotic shock with 2-3 passages through a French Press. Unbroken cells were removed by centrifugation at 5000*g* for 15 min and membranes precipitated by centrifugation at 100000*g* (Beckman Ti50, 38000rpm) for 45 minutes. A Dounce homogenizer was used to re-suspend the membrane pellet in 7.5 ml of 20 mM Tris-HCl (pH 8.0), 1.0 M NaCl and complete protease inhibitor. The suspension was mixed for 2-4 hours, centrifuged at 100000g for 45 min and the pellet resuspended in 7.5 ml of 20mM Tris-HCl (pH 8.0), 1.0M NaCl, 5.0mg/ml CHAPS, 10% (v/v) glycerol and complete protease inhibitor. The solution was mixed overnight, centrifuged at 100000g for 45 minutes and the supernatant dialysed for 6 hours against an appropriately selected buffer. In the case of Orf25.L, the pellet obtained after CHAPS extraction was found to contain the recombinant protein. This fraction, without further purification, was used to immunise mice.

[0285] **FPLC-C:** Identical to FPLC-A, but purification was from the soluble fraction obtained after permeabilising *E.coli* with polymyxin B, rather than after cell disruption.

[0286] **FPLC-D:** A single colony harbouring the plasmid of interest was grown overnight at 37°C in 20 ml of LB/Amp (100 μg/ml) liquid culture. Bacteria were diluted 1:30 in 1.0 L of fresh medium and grown at 30°C until the OD_{550} reached

0.6-0.8. Expression of recombinant protein was induced with IPTG at a final concentration of 1.0mM. After incubation for 3 hours, bacteria were harvested by centrifugation at 8000g for 15 minutes at 4°C. When necessary cells were stored at -20 °C. All subsequent procedures were performed on ice or at 4°C. Cells were resuspended in 20mM Bicine (pH 8.5), 20mM NaCl, 10% (v/v) glycerol, complete protease inhibitor (Boehringer-Mannheim) and disrupted using a Branson Sonifier 450. The sonicate was centrifuged at 8000g for 30 min to sediment unbroken cells and inclusion bodies. The recombinant protein was precipitated from solution between 35% v/v and 70% v/v saturation by the addition of 3.9M $(NH_4)_2SO_4$. The precipitate was sedimented at 8000g for 30 minutes, resuspended in 20 mM Bicine (pH 8.5), 20 mM NaCl, 10% (v/v) glycerol and dialysed against this buffer for 6 hours or overnight. The dialysate was centrifuged at 13000g for 20 min and applied to the FPLC resin. The protein was eluted from the column using a step-wise NaCl gradients. Purification was analysed by SDS-PAGE and protein concentration determined by Bradford method.

Cloning strategy and oligonucleotide design

[0287] Genes coding for antigens of interest were amplified by PCR, using oligonucleotides designed on the basis of the genomic sequence of *N. meningitidis* B MC58. Genomic DNA from strain 2996 was always used as a template in PCR reactions, unless otherwise specified, and the amplified fragments were cloned in the expression vector pET21 b+ (Novagen) to express the protein as C-terminal His-tagged product, or in pET-24b+(Novagen) to express the protein in 'untagged' form (*e.g.* ΔG 287K).

[0288] Where a protein was expressed without a fusion partner and with its own leader peptide (if present), amplification of the open reading frame (ATG to STOP codons) was performed.

[0289] Where a protein was expressed in 'untagged' form, the leader peptide was omitted by designing the 5'-end amplification primer downstream from the predicted leader sequence.

[0290] The melting temperature of the primers used in PCR depended on the number and type of hybridising nucleotides in the whole primer, and was determined using the formulae:

$$T_{m1} = 4\,(G+C) + 2\,(A+T) \qquad \text{(tail excluded)}$$

$$T_{m2} = 64.9 + 0.41\,(\%\ GC) - 600/N \qquad \text{(whole primer)}$$

[0291] The melting temperatures of the selected oligonucleotides were usually 65-70°C for the whole oligo and 50-60°C for the hybridising region alone.

[0292] Oligonucleotides were synthesised using a Perkin Elmer 394 DNA/RNA Synthesizer, eluted from the columns in 2.0ml NH_4OH, and deprotected by 5 hours incubation at 56°C. The oligos were precipitated by addition of 0.3M Na-Acetate and 2 volumes ethanol. The samples were centrifuged and the pellets resuspended in water.

		Sequences	Restriction site
Orf1L	Fwd	CGCGGATCCGCTAGC-AAAACAACCGACAAACGG	NheI
	Rev	CCCGCTCGAG-TTACCAGCGGTAGCCTA	XhoI
Orf1	Fwd	CTAGCTAGC-GGACACACTTATTTCGGCATC	NheI
	Rev	CCCGCTCGAG- TTACCAGCGGTAGCCTAATTTG	XhoI
Orf1LOmpA	Fwd		NdeI-(NheI)
	Rev	CCCGCTCGAG-	XhoI
Orf4L	Fwd	CGCGGATCCCATATG-AAAACCTTCTTCAAAACC	NdeI
	Rev	CCCGCTCGAG-TTATTTGGCTGCGCCTTC	XhoI
Orf7-1L	Fwd	GCGGCATTAAT-ATGTTGAGAAAATTGTTGAAATGG	AseI
	Rev	GCGGCCTCGAG-TTATTTTTTCAAAATATATTTGC	XhoI
Orf9-1L	Fwd	GCGGCCATATG-TTACCTAACCGTTTCAAAATGT	NdeI
	Rev	GCGGCCTCGAG-TTATTTCCGAGGTTTTCGGG	XhoI
Orf23L	Fwd	CGCGGATCCCATATG-ACACGCTTCAAATATTC	NdeI
	Rev	CCCGCTCGAG-TTATTTAAACCGATAGGTAAA	XhoI
Orf25-1 His	Fwd	CGCGGATCCCATATG-GGCAGGGAAGAACCGC	NdeI
	Rev	GCCCAAGCTT-ATCGATGGAATAGCCGCG	HindIII
Orf29-1 b-His (MC58)	Fwd	CGCGGATCCGCTAGC-AACGGTTTGGATGCCCG	NheI
	Rev	CCCGCTCGAG-TTTGTCTAAGTTCCTGATAT CCCGCTCGAG-ATTCCCACCTGCCATC	XhoI
Orf29-1 b-L (MC58)	Fwd	CGCGGATCCGCTAGC-ATGAATTTGCCTATTCAAAAAT	NheI
	Rev	CCCGCTCGAG-TTAATTCCCACCTGCCATC	XhoI
Orf29-1 c-His (MC58)	Fwd	CGCGGATCCGCTAGC-ATGAATTTGCCTATTCAAAAAT	NheI
	Rev	CCCGCTCGAG-TTGGACGATGCCCGCGA	XhoI
Orf29-1 c-L (MC58)	Fwd	CGCGGATCCGCTAGC-ATGAATTTGCCTATTCAAAAAT	NheI
	Rev	CCCGCTCGAG-TTATTGGACGATGCCCGC	XhoI
Orf25L	Fwd	CGCGGATCCCATATG-TATCGCAAACTGATTGC	NdeI
	Rev	CCCGCTCGAG-CTAATCGATGGAATAGCC	XhoI
Orf37L	Fwd	CGCGGATCCCATATG-AAACAGACAGTCAAATG	NdeI
	Rev	CCCGCTCGAG-TCAATAACCCGCCTTCAG	XhoI
Orf38L	Fwd	CGCGGATCCCATATG- TTACGTTTGACTGCTTTAGCCGTATGCACC	NdeI
	Rev	CCCGCTCGAG- TTATTTGCCGCGTTAAAAGCGTCGGCAAC	XhoI
Orf40L	Fwd	CGCGGATCCCATATG-AACAAAATATACCGCAT	NdeI
	Rev	CCCGCTCGAG-TTACCACTGATAACCGAC	XhoI
Orf40.2-His	Fwd	CGCGGATCCCATATG-ACCGATGACGACGATTTAT	NdeI
	Rev	GCCCAAGCTT-CCACTGATAACCGACAGA	HindIII
Orf40.2L	Fwd	CGCGGATCCCATATG-AACAAAATATACCGCAT	NdeI
	Rev	GCCCAAGCTT-TTACCACTGATAACCGAC	HindIII
Orf46-2L	Fwd	GGGAATTCCATATG-GGCATTTCCCGCAAAATATC	NdeI
	Rev	CCCGCTCGAG-TTATTTACTCCTATAACGAGGTCTCTTAAC	XhoI
Orf46-2	Fwd	GGGAATTCCATATG-TCAGATTTGGCAAACGATTCTT	NdeI
	Rev	CCCGCTCGAG-TTATTTACTCCTATAACGAGGTCTCTTAAC	XhoI
Orf46.1L	Fwd	GGGAATTCCATATG-GGCATTTCCCGCAAAATATC	NdeI

	Rev	CCCGCTCGAG-TTACGTATCATATTTCACGTGC	XhoI
orf46. (His-GST)	Fwd	GGGAATTCCATATGCACGTGAAATATGATACGAAG	BamHI-NdeI
	Rev	CCCGCTCGAGTTTACTCCTATAACGAGGTCTCTTAAC	XhoI
orf46.1-His	Fwd	GGGAATTCCATATGTCAGATTTGGCAAACGATTCTT	NdeI
	Rev	CCCGCTCGAGCGTATCATATTTCACGTGC	XhoI
orf46.2-His	Fwd	GGGAATTCCATATGTCAGATTTGGCAAACGATTCTT	NdeI
	Rev	CCCGCTCGAGTTTACTCCTATAACGAGGTCTCTTAAC	XhoI
Orf65-1-(His/GST)	Fwd	CGCGGATCCCATATG-CAAAATGCGTTCAAAATCCC	BamHI-NdeI
(MC58)	Rev	CGCGGATCCCATATG-AACAAAATATACCGCAT CCCGCTCGAG –TTTGCTTTCGATAGAACGG	XhoI
Orf72-1L	Fwd	GCGGCCATATG-GTCATAAAATATACAAATTTGAA	NdeI
	Rev	GCGGCCTCGAG-TTAGCCTGAGACCTTTGCAAATT	XhoI
Orf76-1L	Fwd	GCGGCCATATG-AAACAGAAAAAAACCGCTG	NdeI
	Rev	GCGGCCTCGAG-TTACGGTTTGACACCGTTTTC	XhoI
Orf83.1L	Fwd	CGCGGATCCCATATG-AAAACCCTGCTCCTC	NdeI
	Rev	CCCGCTCGAG-TTATCCTCCTTTGCGGC	XhoI
Orf85-2L	Fwd	GCGGCCATATG-GCAAAAATGATGAAATGGG	NdeI
	Rev	GCGGCCTCGAG-TTATCGGCGCGGCGGGCC	XhoI
Orf91L (MC58)	Fwd	GCGGCCATATGAAAAAATCCTCCCTCATCA	NdeI
	Rev	GCGGCCTCGAGTTATTTGCCGCCGTTTTTGGC	XhoI
Orf91-His(MC58)	Fwd	GCGGCCATATGGCCCCTGCCGACGCGGTAAG	NdeI
	Rev	GCGGCCTCGAGTTTGCCGCCGTTTTTGGCTTTC	XhoI
Orf97-1L	Fwd	GCGGCCATATG-AAACACATACTCCCCCTGA	NdeI
	Rev	GCGGCCTCGAG-TTATTCGCCTACGGTTTTTTG	XhoI
Orf119L (MC58)	Fwd	GCGGCCATATGATTTACATCGTACTGTTTC	NdeI
	Rev	GCGGCCTCGAGTTAGGAGAACAGGCGCAATGC	XhoI
Orf119-His(MC58)	Fwd	GCGGCCATATGTACAACATGTATCAGGAAAAC	NdeI
	Rev	GCGGCCTCGAGGGAGAACAGGCGCAATGCGG	XhoI
Orf137.1 (His-GST) (MC58)	Fwd	CGCGGATCCGCTAGCTGCGGCACGGCGGG	BamHI-NheI
	Rec	CCCGCTCGAGATAACGGTATGCCGCCAG	XhoI
Orf143-1L	Fwd	CGCGGATCCCATATG-GAATCAACACTTTCAC	NdeI
	Rev	CCCGCTCGAG-TTACACGCGGTTGCTGT	XhoI
008	Fwd	CGCGGATCCCATATG-AACAACAGACATTTTG	NdeI
	Rev	CCCGCTCGAG-TTACCTGTCCGGTAAAAG	XhoI
050-1(48)	Fwd	CGCGGATCCGCTAGC-ACCGTCATCAAACAGGAA	NheI
	Rev	CCCGCTCGAG-TCAAGATTCGACGGGGA	XhoI
105	Fwd	CGCGGATCCCATATG-TCCGCAAACGAATACG	NdeI
	Rev	CCCGCTCGAG-TCAGTGTTCTGCCAGTTT	XhoI
111L	Fwd	CGCGGATCCCATATG-CCGTCTGAAACACG	NdeI
	Rev	CCCGCTCGAG-TTAGCGGAGCAGTTTTTC	XhoI
117-1	Fwd	CGCGGATCCCATATG-ACCGCCATCAGCC	NdeI
	Rev	CCCGCTCGAG-TTAAAGCCGGGTAACGC	XhoI
121-1	Fwd	GCGGCCATATG-GAAACACAGCTTTACATCGG	NdeI
	Rev	GCGGCCTCGAG-TCAATAATAATATCCCGCG	XhoI

122-1	Fwd	GCGGCCATATG-ATTAAAATCCGCAATATCC	NdeI
	Rev	GCGGCCTCGAG-TTAAATCTTGGTAGATTGGATTTGG	XhoI
128-1	Fwd	GCGGCCATATG-ACTGACAACGCACTGCTCC	NdeI
	Rev	GCGGCCTCGAG-TCAGACCGCGTTGTCGAAAC	XhoI
148	Fwd	CGCGGATCCCATATG-GCGTTAAAAACATCAAA	NdeI
	Rev	CCCGCTCGAG-TCAGCCCTTCATACAGC	XhoI
149.1L (MC58)	Fwd	GCGGCATTAATGGCACAAACTACACTCAAACC	AseI
	Rev	GCGGCCTCGAGTTAAAACTTCACGTTCACGCCG	XhoI
149.1-His(MC58)	Fwd	GCGGCATTAATGCATGAAACTGAGCAATCGGTGG	AseI
	Rev	GCGGCCTCGAGAAACTTCACGTTCACGCCGCCGGTAAA	XhoI
205 (His-GST) (MC58)	Fwd	CGCGGATCCCATATGGGCAAATCCGAAAATACG	BamHI-NdeI
	Rev	CCCGCTCGAGATAATGGCGGCGGCGG	XhoI
206L	Fwd	CGCGGATCCCATATG-TTTCCCCCCGACAA	NdeI
	Rev	CCCGCTCGAG-TCATTCTGTAAAAAAAGTATG	XhoI
214 (His-GST) (MC58)	Fwd	CGCGGATCCCATATGCTTCAAAGCGACAGCAG	BamHI-NdeI
	Rev	CCCGCTCGAGTTCGGATTTTTGCGTACTC	XhoI
216	Fwd	CGCGGATCCCATATG-GCAATGGCAGAAAACG	NdeI
	Rev	CCCGCTCGAG-CTATACAATCCGTGCCG	XhoI
225-1L	Fwd	CGCGGATCCCATATG-GATTCTTTTTTCAAACC	NdeI
	Rev	CCCGCTCGAG-TCAGTTCAGAAAGCGGG	XhoI
235L	Fwd	CGCGGATCCCATATG-AAACCTTTGATTTTAGG	NdeI
	Rev	CCCGCTCGAG-TTATTTGGGCTGCTCTTC	XhoI
243	Fwd	CGCGGATCCCATATG-GTAATCGTCTGGTTG	NdeI
	Rev	CCCGCTCGAG-CTACGACTTGGTTACCG	XhoI
247-1L	Fwd	GCGGCCATATG-AGACGTAAAATGCTAAAGCTAC	NdeI
	Rev	GCGGCCTCGAG-TCAAAGTGTTCTGTTTGCGC	XhoI
264-His	Fwd	GCCGCCATATG-TTGACTTTAACCCGAAAAA	NdeI
	Rev	GCCGCCTCGAG-GCCGGCGGTCAATACCGCCCGAA	XhoI
270 (His-GST) (MC58)	Fwd	CGCGGATCCCATATGGCGCAATGCGATTTGAC	BamHI-NdeI
	Rev	CCCGCTCGAGTTCGGCGGTAAATGCCG	XhoI
274L	Fwd	GCGGCCATATG-GCGGGGCCGATTTTTGT	NdeI
	Rev	GCGGCCTCGAG-TTATTTGCTTTCAGTATTATTG	XhoI
283L	Fwd	GCGGCCATATG-AACTTTGCTTTATCCGTCA	NdeI
	Rev	GCGGCCTCGAG-TTAACGGCAGTATTTGTTTAC	XhoI
285-His	Fwd	CGCGGATCCCATATGGGTTTGCGCTTCGGGC	BamHI
	Rev	GCCCAAGCTTTTTTCCTTTGCCGTTTCCG	HindIII
286-His (MC58)	Fwd	CGCGGATCCCATATG-GCCGACCTTTCCGAAAA	NdeI
	Rev	CCCGCTCGAG-GAAGCGCGTTCCCAAGC	XhoI
286L (MC58)	Fwd	CGCGGATCCCATATG-CACGACACCCGTAC	NdeI
	Rev	CCCGCTCGAG-TTAGAAGCGCGTTCCCAA	XhoI
287L	Fwd	CTAGCTAGC-TTTAAACGCAGCGTAATCGCAATGG	NheI
	Rev	CCCGCTCGAG-TCAATCCTGCTCTTTTTTGCC	XhoI

287	Fwd	CTAGCTAGC-GGGGGCGGCGGTGGCG	NheI
	Rev	CCCGCTCGAG-TCAATCCTGCTCTTTTTTGCC	XhoI
287LOrf4	Fwd	CTAGCTAGCGCTCATCCTCGCCGCC-TGCGGGGGCGGCGGT	NheI
	Rev	CCCGCTCGAG-TCAATCCTGCTCTTTTTTGCC	XhoI
287-fu	Fwd	CGGGGATCC-GGGGGCGGCGGTGGCG	BamHI
	Rev	CCCGCTCGAG-TCAATCCTGCTCTTTTTTGCC	XhoI
287-His	Fwd	CTAGCTAGC-GGGGGCGGCGGTGGCG	NheI
	Rev	CCCGCTCGAG-ATCCTGCTCTTTTTTGCC *	XhoI
287-His(2996)	Fwd	CTAGCTAGC-TGCGGGGGCGGCGGTGGCG	NheI
	Rev	CCCGCTCGAG-ATCCTGCTCTTTTTTGCC	XhoI
Δ1 287-His	Fwd	CGCGGATCCGCTAGC-CCCGATGTTAAATCGGC §	NheI
Δ2 287-His	Fwd	CGCGGATCCGCTAGC-CAAGATATGGCGGCAGT §	NheI
Δ3 287-His	Fwd	CGCGGATCCGCTAGC-GCCGAATCCGCAAATCA §	NheI
Δ4 287-His	Fwd	CGCGCTAGC-GGAAGGGTTGATTTGGCTAATGG §	NheI
Δ4 287MC58-His	Fwd	CGCGCTAGC-GGAAGGGTTGATTTGGCTAATGG §	NheI
287a-His	Fwd	CGCCATATG-TTTAAACGCAGCGTAATCGC	NdeI
	Rev	CCCGCTCGAG-AAAATTGCTACCGCCATTCGCAGG	XhoI
287b-His	Fwd	CGCCATATG-GGAAGGGTTGATTTGGCTAATGG	NdeI
287b-2996-His	Rev	CCCGCTCGAG-CTTGTCTTTATAAATGATGACATATTTG	XhoI
287b-MC58-His	Rev	CCCGCTCGAG-TTTATAAAAGATAATATATTGATTGATTCC	XhoI
287c-2996-His	Fwd	CGCGCTAGC-ATGCCGCTGATTCCCGTCAATC §	NheI
'287^{untagged}'(2996)	Fwd	CTAGCTAGC-GGGGGCGGCGGTGGCG	NheI
	Rev	CCCGCTCGAG-TCAATCCTGCTCTTTTTTGCC	XhoI
ΔG287-His *	Fwd	CGCGGATCCGCTAGC-CCCGATGTTAAATCGGC	NheI
	Rev	CCCGCTCGAG-ATCCTGCTCTTTTTTGCC	XhoI
ΔG287K(2996)	Fwd	CGCGGATCCGCTAGC-CCCGATGTTAAATCGGC	NheI
	Rev	CCCGCTCGAG-TCAATCCTGCTCTTTTTTGCC	XhoI
ΔG 287-L	Fwd	CGCGGATCCGCTAGC-TTTGAACGCAGTGTGATTGCAATGGCTTGTATTTTTGCC CTTTCAGCCTGT TCGCCCGATGTTAAATCGGCG	NheI
	Rev	CCCGCTCGAG-TCAATCCTGCTCTTTTTTGCC	XhoI
ΔG 287-Orf4L	Fwd	CGCGGATCCGCTAGC-AAAACCTTCTTCAAAACCCTTTCCGCCGCCGCACTCGCG CTCATCCTCGCCGCCTGC TCGCCCGATGTTAAATCG	NheI
	Rev	CCCGCTCGAG-TCAATCCTGCTCTTTTTTGCC	XhoI
292L	Fwd	CGCGGATCCCATATG-AAAACCAAGTTAATCAAA	NdeI
	Rev	CCCGCTCGAG-TTATTGATTTTTGCGGATGA	XhoI
308-1	Fwd	CGCGGATCCCATATG-TTAAATCGGGTATTTTATC	NdeI
	Rev	CCCGCTCGAG-TTAATCCGCCATTCCCTG	XhoI
401L	Fwd	GCGGCCATATG-AAATTACAACAATTGGCTG	NdeI
	Rev	GCGGCCTCGAG-TTACCTTACGTTTTTCAAAG	XhoI
406L	Fwd	CGCGGATCCCATATG-CAAGCACGGCTGCT	NdeI
	Rev	CCCGCTCGAG-TCAAGGTTGTCCTTGTCTA	XhoI
502-1L	Fwd	CGCGGATCCCATATG-ATGAAACCGCACAAC	NdeI
	Rev	CCCGCTCGAG-TCAGTTGCTCAACACGTC	XhoI

502-A (His-GST)	Fwd	CGCGGATCCCATATGGTAGACGCGCTTAAGCA	BamHI-NdeI
	Rev	CCCGCTCGAGAGCTGCATGGCGGCG	XhoI
503-1L	Fwd	CGCGGATCCCATATG-GCACGGTCGTTATAC	NdeI
	Rev	CCCGCTCGAG-CTACCGCGCATTCCTG	XhoI
519-1L	Fwd	GCGGCCATATG-GAATTTTTCATTATCTTGTT	NdeI
	Rev	GCGGCCTCGAG-TTATTTGGCGGTTTTGCTGC	XhoI
525-1L	Fwd	GCGGCCATATG-AAGTATGTCCGGTTATTTTTC	NdeI
	Rev	GCGGCCTCGAG-TTATCGGCTTGTGCAACGG	XhoI
529-(His/GST) (MC58)	Fwd	CGCGGATCCGCTAGC-TCCGGCAGCAAAACCGA	Bam HI-NheI
	Rev	GCCCAAGCTT-ACGCAGTTCGGAATGGAG	HindIII
552L	Fwd	GCCGCCATATGTTGAATATTAAACTGAAAACCTTG	NdeI
	Rev	GCCGCCTCGAGTTATTTCTGATGCCTTTTCCC	XhoI
556L	Fwd	GCCGCCATATGGACAATAAGACCAAACTG	NdeI
	Rev	GCCGCCTCGAGTTAACGGTGCGGACGTTTC	XhoI
557L	Fwd	CGCGGATCCCATATG-AACAAACTGTTTCTTAC	NdeI
	Rev	CCCGCTCGAG-TCATTCCGCCTTCAGAAA	XhoI
564ab-(His/GST) (MC58)	Fwd	CGCGGATCCCATATG-CAAGGTATCGTTGCCGACAAATCCGCACCT	BamHI-NdeI
	Rev	CCCGCTCGAG-AGCTAATTGTGCTTGGTTTGCAGATAGGAGTT	XhoI
564abL (MC58)	Fwd	CGCGGATCCCATATG-AACCGCACCCTGTACAAAGTTGTATTTAACAAACATC	NdeI
	Rev	CCCGCTCGAG-TTAAGCTAATTGTGCTTGGTTTGCAGATAGGAGTT	XhoI
564b-(His/GST)(MC58)	Fwd	CGCGGATCCCATATG-ACGGGAGAAAATCATGCGGTTTCACTTCATG	BamHI-NdeI
	Rev	CCCGCTCGAG-AGCTAATTGTGCTTGGTTTGCAGATAGGAGTT	XhoI
564c-(His/GST)(MC58)	Fwd	CGCGGATCCCATATG-GTTTCAGACGGCCTATACAACCAACATGGTGAAATT	BamHI-NdeI
	Rev	CCCGCTCGAG-GCGGTAACTGCCGCTTGCACTGAATCCGTAA	XhoI
564bc-(His/GST)(MC58)	Fwd	CGCGGATCCCATATG-ACGGGAGAAAATCATGCGGTTTCACTTCATG	BamHI-NdeI
	Rev	CCCGCTCGAG-GCGGTAACTGCCGCTTGCACTGAATCCGTAA	XhoI
564d-(His/GST)(MC58)	Fwd	CGCGGATCCCATATG-CAAAGCAAAGTCAAAGCAGACCATGCCTCCGTAA	BamHI-NdeI
	Rev	CCCGCTCGAG-TCTTTTCCTTTCAATTATAACTTTAGTAGGTTCAATTTTGGTCCCC	XhoI
564cd-(His/GST)(MC58)	Fwd	CGCGGATCCCATATG-GTTTCAGACGGCCTATACAACCAACATGGTGAAATT	BamHI-NdeI
	Rev	CCCGCTCGAG-TCTTTTCCTTTCAATTATAACTTTAGTAGGTTCAATTTTGGTCCCC	XhoI
570L	Fwd	GCGGCCATATG-ACCCGTTTGACCCGCG	NdeI
	Rev	GCGGCCTCGAG-TCAGCGGGCGTTCATTTCTT	XhoI
576-1L	Fwd	CGCGGATCCCATATG-AACACCATTTTCAAAATC	NdeI
	Rev	CCCGCTCGAG-TTAATTTACTTTTTTGATGTCG	XhoI

580L	Fwd	GCGGCCATATG-GATTCGCCCAAGGTCGG	NdeI
	Rev	GCGGCCTCGAG-CTACACTTCCCCCGAAGTGG	XhoI
583L	Fwd	CGCGGATCCCATATG-ATAGTTGACCAAAGCC	NdeI
	Rev	CCCGCTCGAG-TTATTTTTCCGATTTTTCGG	XhoI
593	Fwd	GCGGCCATATG-CTTGAACTGAACGGACT	NdeI
	Rev	GCGGCCTCGAG-TCAGCGGAAGCGGACGATT	XhoI
650 (His-GST) (MC58)	Fwd	CGCGGATCCCATATGTCCAAACTCAAAACCATCG	BamHI-NdeI
	Rev	CCCGCTCGAGGCTTCCAATCAGTTTGACC	XhoI
652	Fwd	GCGGCCATATG-AGCGCAATCGTTGATATTTTC	NdeI
	Rev	GCGGCCTCGAG-TTATTTGCCCAGTTGGTAGAATG	XhoI
664L	Fwd	GCGGCCATATG-GTGATACATCCGCACTACTTC	NdeI
	Rev	GCGGCCTCGAG-TCAAAATCGAGTTTTACACCA	XhoI
726	Fwd	GCGGCCATATG-ACCATCTATTTCAAAAACGG	NdeI
	Rev	GCGGCCTCGAG-TCAGCCGATGTTTAGCGTCCATT	XhoI
741-His(MC58)	Fwd	CGCGGATCCCATATG-AGCAGCGGAGGGGGTG	NdeI
	Rev	CCCGCTCGAG-TTGCTTGGCGGCAAGGC	XhoI
ΔG741-His(MC58)	Fwd	CGCGGATCCCATATG-GTCGCCGCCGACATCG	NdeI
	Rev	CCCGCTCGAG-TTGCTTGGCGGCAAGGC	XhoI
686-2-(His/GST)	Fwd	CGCGGATCCCATATG-GGCGGTTCGGAAGGCG	BamHI-NdeI
(MC58)	Rev	CCCGCTCGAG-TTGAACACTGATGTCTTTTCCGA	XhoI
719-(His/GST)	Fwd	CGCGGATCCGCTAGC-AAACTGTCGTTGGTGTTAAC	BamHI-NheI
(MC58)	Rev	CCCGCTCGAG-TTGACCCGCTCCACGG	XhoI
730-His (MC58)	Fwd	GCCGCCATATGGCGGACTTGGCGCAAGACCC	NdeI
	Rev	GCCGCCTCGAGATCTCCTAAACCTGTTTTAACAATGCCG	XhoI
730A-His (MC58)	Fwd	GCCGCCATATGGCGGACTTGGCGCAAGACCC	NdeI
	Rev	GCGGCCTCGAGCTCCATGCTGTTGCCCCAGC	XhoI
730B-His (MC58)	Fwd	GCCGCCATATGGCGGACTTGGCGCAAGACCC	NdeI
	Rev	GCGGCCTCGAGAAAATCCCCGCTAACCGCAG	XhoI
741-His	Fwd	CGCGGATCCCATATG-AGCAGCGGAGGGGGTG	NdeI
(MC58)	Rev	CCCGCTCGAG-TTGCTTGGCGGCAAGGC	XhoI
ΔG741-His	Fwd	CGCGGATCCCATATG-GTCGCCGCCGACATCG	NdeI
(MC58)	Rev	CCCGCTCGAG-TTGCTTGGCGGCAAGGC	XhoI
743 (His-GST)	Fwd	CGCGGATCCCATATGGACGGTGTTGTGCCTGTT	BamHI-NdeI
	Rev	CCCGCTCGAGCTTACGGATCAAATTGACG	XhoI
757 (His-GST) (MC58)	Fwd	CGCGGATCCCATATGGGCAGCCAATCTGAAGAA	BamHI-NdeI
	Rev	CCCGCTCGAGCTCAGCTTTTGCCGTCAA	XhoI
759-His/GST	Fwd	CGCGGATCCGCTAGC-TACTCATCCATTGTCCGC	BamHI-NheI
(MC58)	Rev	CCCGCTCGAG-CCAGTTGTAGCCTATTTTG	XhoI
759L	Fwd	CGCGGATCCGCTAGC-ATGCGCTTCACACACAC	NheI
(MC58)	Rev	CCCGCTCGAG-TTACCAGTTGTAGCCTATTT	XhoI
760-His	Fwd	GCCGCCATATGGCACAAACGGAAGGTTTGGAA	NdeI
	Rev	GCCGCCTCGAGAAAACTGTAACGCAGGTTTGCCGTC	XhoI
769-His (MC58)	Fwd	GCGGCCATATGGAAGAAACACCGCGCGAACCG	NdeI

	Rev	GCGGCCTCGAGGAACGTTTTATTAAACTCGAC	XhoI
907L	Fwd	GCGGCCATATG-AGAAAACCGACCGATACCCTA	NdeI
	Rev	GCGGCCTCGAG-TCAACGCCACTGCCAGCGGTTG	XhoI
911L	Fwd	CGCGGATCCCATATG-AAGAAGAACATATTGGAATTTTGGGTCGGACTG	NdeI
	Rev	CCCGCTCGAG-TTATTCGGCGGCTTTTTCCGCATTGCCG	XhoI
911LOmpA	Fwd	GGGAATTCCATATGAAAAAGACAGCTATCGCGATTGCA GTGGCACTGGCTGGTTTCGCTACCGTAGCGCAGGCCGC TAGC-GCTTTCCGCGTGGCCGGCGGTGC	NdeI-(NheI)
	Rev	CCCGCTCGAG-TTATTCGGCGGCTTTTTCCGCATTGCCG	XhoI
911LPelB	Fwd	CATGCCATGG-CTTTCCGCGTGGCCGGCGGTGC	NcoI
	Rev	CCCGCTCGAG-TTATTCGGCGGCTTTTTCCGCATTGCCG	XhoI
913-His/GST	Fwd	CGCGGATCCCATATG-TTTGCCGAAACCCGCC	BamHI-NdeI
(MC58)	Rev	CCCGCTCGAG-AGGTTGTGTTCCAGGTTG	XhoI
913L	Fwd	CGCGGATCCCATATG-AAAAAAACCGCCTATG	NdeI
(MC58)	Rev	CCCGCTCGAG-TTAAGGTTGTGTTCCAGG	XhoI
919L	Fwd	CGCGGATCCCATATG-AAAAAATACCTATTCCGC	NdeI
	Rev	CCCGCTCGAG-TTACGGGCGGTATTCGG	XhoI
919	Fwd	CGCGGATCCCATATG-CAAAGCAAGAGCATCCAAA	NdeI
	Rev	CCCGCTCGAG-TTACGGGCGGTATTCGG	XhoI
919L Orf4	Fwd	GGGAATTCCATATGAAAACCTTCTTCAAAACCCTTTCCG CCGCCGCGCTAGCGCTCATCCTCGCCGCC- TGCCAAAGCAAGAGCATC	NdeI-(NheI)
	Rev	CCCGCTCGAG-TTACGGGCGGTATTCGGGCTTCATACCG	XhoI
(919)-287fusion	Fwd	CGCGGATCCGTCGAC-TGTGGGGGCGGCGGTGGC	SalI
	Rev	CCCGCTCGAG-TCAATCCTGCTCTTTTTTGCC	XhoI
920-1L	Fwd	GCGGCCATATG-AAGAAAACATTGACACTGC	NdeI
	Rev	GCGGCCTCGAG-TTAATGGTGCGAATGACCGAT	XhoI
925-His/GST (MC58) GATE	Fwd	ggggacaagtttgtacaaaaaagcaggctTGCGGCAAGGATGCCGG	*attB1*
	Rev	ggggaccactttgtacaagaaagctgggtCTAAAGCAACAATGCCGG	*attB2*
926L	Fwd	CGCGGATCCCATATG-AAACACACCGTATCC	NdeI
	Rev	CCCGCTCGAG-TTATCTCGTGCGCGCC	XhoI
927-2-(His/GST)	Fwd	CGCGGATCCCATATG-AGCCCCGCGCCGATT	BamHI-NdeI
(MC58)	Rev	CCCGCTCGAG-TTTTGTGCGGTCAGGCG	XhoI
932-His/GST (MC58) GATE	Fwd	ggggacaagtttgtacaaaaaagcaggctTGTTCGTTTGGGGGATTTAA ACCAAACCAAATC	*attB1*
935 (His-GST) (MC58)	For	CGCGGATCCCATATGGCGGATGCGCCCGCG	BamHI-NdeI
	Rev	CCCGCTCGAGAAACCGCCAATCCGCC	XhoI
	Rev	ggggaccactttgtacaagaaagctgggtTCATTTTGTTTTTCCTTCTTCT CGAGGCCATT	*attB2*
936-1L	Fwd	CGCGGATCCCATATG-AAACCCAAACCGCAC	NdeI
	Rev	CCCGCTCGAG-TCAGCGTTGGACGTAGT	XhoI
953L	Fwd	GGGAATTCCATATG-AAAAAAATCATCTTCGCCG	NdeI
	Rev	CCCGCTCGAG-TTATTGTTTGGCTGCCTCGAT	XhoI
953-fu	Fwd	GGGAATTCCATATG-GCCACCTACAAAGTGGACG	NdeI
	Rev	CGGGGATCC-TTGTTTGGCTGCCTCGATTTG	BamHI

954 (His-GST) (MC58)	Fwd	CGCGGATCCCATATGCAAGAACAATCGCAGAAAG	BamHI-NdeI
	Rev	CCCGCTCGAGTTTTTCGGCAAATTGGCTT	XhoI
958-His/GST (MC58) GATE	Fwd	ggggacaagtttgtacaaaaaagcaggctGCCGATGCCGTTGCGG	*attB1*
	Rev	ggggaccactttgtacaagaaagctgggtTCAGGGTCGTTTGTTGCG	*attB2*
961L	Fwd	CGCGGATCCCATATG-AAACACTTTCCATCC	NdeI
	Rev	CCCGCTCGAG-TTACCACTCGTAATTGAC	XhoI
961	Fwd	CGCGGATCCCATATG-GCCACAAGCGACGAC	NdeI
	Rev	CCCGCTCGAG-TTACCACTCGTAATTGAC	XhoI
961 c (His/GST)	Fwd	CGCGGATCCCATATG-GCCACAAACGACG	BamHI-NdeI
	Rev	CCCGCTCGAG-ACCCACGTTGTAAGGTTG	XhoI
961 c-(His/GST)	Fwd	CGCGGATCCCATATG-GCCACAAGCGACGACGA	BamHI-NdeI
(MC58)	Rev	CCCGCTCGAG-ACCCACGTTGTAAGGTTG	XhoI
961 c-L	Fwd	CGCGGATCCCATATG-ATGAAACACTTTCCATCC	NdeI
	Rev	CCCGCTCGAG-TTAACCCACGTTGTAAGGT	XhoI
961 c-L	Fwd	CGCGGATCCCATATG-ATGAAACACTTTCCATCC	NdeI
(MC58)	Rev	CCCGCTCGAG-TTAACCCACGTTGTAAGGT	XhoI
961 d (His/GST)	Fwd	CGCGGATCCCATATG-GCCACAAACGACG	BamHI-NdeI
	Rev	CCCGCTCGAG-GTCTGACACTGTTTTATCC	XhoI
961 Δ1-L	Fwd	CGCGGATCCCATATG-ATGAAACACTTTCCATCC	NdeI
	Rev	CCCGCTCGAG-TTATGCTTTGGCGGCAAAG	XhoI
fu 961-...	Fwd	CGCGGATCCCATATG- GCCACAAACGACGAC	NdeI
	Rev	CGCGGATCC-CCACTCGTAATTGACGCC	BamHI
fu 961-...	Fwd	CGCGGATCCCATATG-GCCACAAGCGACGAC	NdeI
(MC58)	Rev	CGCGGATCC-CCACTCGTAATTGACGCC	BamHI
fu 961 c -...	Fwd	CGCGGATCCCATATG-GCCACAAACGACGAC	NdeI
	Rev	CGCGGATCC -ACCCACGTTGTAAGGTTG	BamHI
fu 961 c-L-...	Fwd	CGCGGATCCCATATG- ATGAAACACTTTCCATCC	NdeI
	Rev	CGCGGATCC -ACCCACGTTGTAAGGTTG	BamHI
fu (961)-741(MC58)-His	Fwd	CGCGGATCC -GGAGGGGGTGGTGTCG	BamHI
	Rev	CCCGCTCGAG-TTGCTTGGCGGCAAGGC	XhoI
fu (961)-983-His	Fwd	CGCGGATCC - GGCGGAGGCGGCACTT	BamHI
	Rev	CCCGCTCGAG-GAACCGGTAGCCTACG	XhoI
fu (961)- Orf46.1-His	Fwd	CGCGGATCCGGTGGTGGTGGT-TCAGATTTGGCAAACGATTC	BamHI
	Rev	CCCGCTCGAG-CGTATCATATTTCACGTGC	XhoI
fu (961 c-L)-741(MC58)	Fwd	CGCGGATCC -GGAGGGGGTGGTGTCG	BamHI
	Rev	CCCGCTCGAG-TTATTGCTTGGCGGCAAG	XhoI
fu (961c-L)-983	Fwd	CGCGGATCC - GGCGGAGGCGGCACTT	BamHI
	Rev	CCCGCTCGAG-TCAGAACCGGTAGCCTAC	XhoI
fu (961c-L)-Orf46.1	Fwd	CGCGGATCCGGTGGTGGTGGT-TCAGATTTGGCAAACGATTC	BamHI
	Rev	CCCGCTCGAG-TTACGTATCATATTTCACGTGC	XhoI
961-(His/GST)	Fwd	CGCGGATCCCATATG-GCCACAAGCGACGACG	BamHI-NdeI

(MC58)	Rev	CCCGCTCGAG-CCACTCGTAATTGACGCC	XhoI
961 Δ1-His	Fwd	CGCGGATCCCATATG-GCCACAAACGACGAC	NdeI
	Rev	CCCGCTCGAG-TGCTTTGGCGGCAAAGTT	XhoI
961a-(His/GST)	Fwd	CGCGGATCCCATATG-GCCACAAACGACGAC	BamHI-NdeI
	Rev	CCCGCTCGAG-TTTAGCAATATTATCTTTGTTCGTAGC	XhoI
961b-(His/GST)	Fwd	CGCGGATCCCATATG-AAAGCAAACCGTGCCGA	BamHI-NdeI
	Rev	CCCGCTCGAG-CCACTCGTAATTGACGCC	XhoI
961-His/GST GATE	Fwd	ggggacaagtttgtacaaaaaagcaggctGCAGCCACAAACGACGACG ATGTTAAAAAAGC	*attB1*
	Rev	ggggaccactttgtacaagaaagctgggtTTACCACTCGTAATTGACGC CGACATGGTAGG	*attB2*
982	Fwd	GCGGCCATATG-GCAGCAAAAGACGTACAGTT	NdeI
	Rev	GCGGCCTCGAG-TTACATCATGCCGCCCATACCA	XhoI
983-His (2996)	Fwd	CGCGGATCCGCTAGC-TTAGGCGGCGGCGGAG	NheI
	Rev	CCCGCTCGAG-GAACCGGTAGCCTACG	XhoI
ΔG983-His (2996)	Fwd	CCCCTAGCTAGC-ACTTCTGCGCCCGACTT	NheI
	Rev	CCCGCTCGAG-GAACCGGTAGCCTACG	XhoI
983-His	Fwd	CGCGGATCCGCTAGC-TTAGGCGGCGGCGGAG	NheI
	Rev	CCCGCTCGAG-GAACCGGTAGCCTACG	XhoI
ΔG983-His	Fwd	CGCGGATCCGCTAGC-ACTTCTGCGCCCGACTT	NheI
	Rev	CCCGCTCGAG-GAACCGGTAGCCTACG	XhoI
983L	Fwd	CGCGGATCCGCTAGC- CGAACGACCCCAACCTTCCCTACAAAAACTTTCAA	NheI
	Rev	CCCGCTCGAG-TCAGAACCGACGTGCCAAGCCGTTC	XhoI
987-His (MC58)	Fwd	GCCGCCATATGCCCCCACTGGAAGAACGGACG	NdeI
	Rev	GCCGCCTCGAGTAATAAACCTTCTATGGGCAGCAG	XhoI
989-(His/GST)	Fwd	CGCGGATCCCATATG-TCCGTCCACGCATCCG	BamHI-NdeI
(MC58)	Rev	CCCGCTCGAG-TTTGAATTTGTAGGTGTATTG	XhoI
989L	Fwd	CGCGGATCCCATATG-ACCCCTTCCGCACT	NdeI
(MC58)	Rev	CCCGCTCGAG-TTATTTGAATTTGTAGGTGTAT	XhoI
CrgA-His	Fwd	CGCGGATCCCATATG-AAAACCAATTCAGAAGAA	NdeI
(MC58)	Rev	CCCGCTCGAG-TCCACAGAGATTGTTTCC	XhoI
PilC1-ES	Fwd	GATGCCCGAAGGGCGGG	
(MC58)	Rev	GCCCAAGCTT-TCAGAAGAAGACTTCACGC	
PilC1-His	Fwd	CGCGGATCCCATATG-CAAACCCATAAATACGCTATT	NdeI
(MC58)	Rev	GCCCAAGCTT-GAAGAAGACTTCACGCCAG	HindIII
Δ1PilC1-His	Fwd	CGCGGATCCCATATG-GTCTTTTTCGACAATACCGA	NdeI
(MC58)	Rev	GCCCAAGCTT-	HindIII
PilC1L	Fwd	CGCGGATCCCATATG-AATAAAACTTTAAAAAGGCGG	NdeI
(MC58)	Rev	GCCCAAGCTT-TCAGAAGAAGACTTCACGC	HindIII
ΔGTbp2-His	Fwd	CGCGAATCCCATATG-TTCGATCTTGATTCTGTCGA	NdeI
(MC58)	Rev	CCCGCTCGAG-TCGCACAGGCTGTTGGCG	XhoI
Tbp2-His	Fwd	CGCGAATCCCATATG-TTGGGCGGAGGCGGCAG	NdeI
(MC58)	Rev	CCCGCTCGAG-TCGCACAGGCTGTTGGCG	XhoI
Tbp2-His(MC58)	Fwd	CGCGAATCCCATATG-TTGGGCGGAGGCGGCAG	NdeI
	Rev	CCCGCTCGAG-TCGCACAGGCTGTTGGCG	XhoI

NMB0109-(His/GST)	Fwd	CGCGGATCCCATATG-GCAAATTTGGAGGTGCGC	BamHI-NdeI
(MC58)	Rev	CCCGCTCGAG-TTCGGAGCGGTTGAAGC	XhoI
NMB0109L	Fwd	CGCGGATCCCATATG-CAACGTCGTATTATAACCC	NdeI
(MC58)	Rev	CCCGCTCGAG-TTATTCGGAGCGGTTGAAG	XhoI
NMB0207-(His/GST)	Fwd	CGCGGATCCCATATG-GGCATCAAAGTCGCCATCAACGGCTAC	BamHI-NdeI
(MC58)	Rev	CCCGCTCGAG-TTTGAGCGGGCGCACTTCAAGTCCG	XhoI
NMB0462-(His/GST)	Fwd	CGCGGATCCCATATG-GGCGGCAGCGAAAAAAAC	BamHI-NdeI
(MC58)	Rev	CCCGCTCGAG-GTTGGTGCCGACTTTGAT	XhoI
NMB0623-(His/GST)	Fwd	CGCGGATCCCATATG-GGCGGCGGAAGCGATA	BamHI-NdeI
(MC58)	Rev	CCCGCTCGAG-TTTGCCCGCTTTGAGCC	XhoI
NMB0625 (His-GST)(MC58)	Fwd	CGCGGATCCCATATGGGCAAATCCGAAAATACG	BamHI-NdeI
	Rev	CCCGCTCGAGCATCCCGTACTGTTTCG	XhoI
NMB0634 (His/GST)(MC58)	Fwd	ggggacaagtttgtacaaaaaagcaggctCCGACATTACCGTGTACAACGGCCAACAAAGAA	*attB1*
	Rev	ggggaccactttgtacaagaaagctgggtCTTATTTCATACCGGCTTGCTCAAGCAGCCGG	*attB2*
NMB0776-His/GST (MC58) GATE	Fwd	ggggacaagtttgtacaaaaaagcaggctGATACGGTGTTTTCCTGTAAAACGGACAACAA	*attB1*
	Rev	ggggaccactttgtacaagaaagctgggtCTAGGAAAAATCGTCATCGTTGAAATTCGCC	*attB2*
NMB1115-His/GST (MC58) GATE	Fwd	ggggacaagtttgtacaaaaaagcaggctATGCACCCCATCGAAACC	*attB1*
	Rev	ggggaccactttgtacaagaaagctgggtCTAGTCTTGCAGTGCCTC	*attB2*
NMB1343-(His/GST)	Fwd	CGCGGATCCCATATG-GGAAATTTCTTATATAGAGGCATTAG	BamHI-NdeI
(MC58)	Rev	CCCGCTCGAG-GTTAATTTCTATCAACTCTTTAGCAATAAT	XhoI
NMB1369 (His-GST (MC58)	Fwd	CGCGGATCCCATATGGCCTGCCAAGACGACA	BamHI-NdeI
	Rev	CCCGCTCGAGCCGCCTCCTGCCGAAA	XhoI
NMB1551 (His-GST)(MC58)	Fwd	CGCGGATCCCATATGGCAGAGATCTGTTTGATAA	BamHI-NdeI
	Rev	CCCGCTCGAGCGGTTTTCCGCCCAATG	XhoI
NMB1899 (His-GST) (MC58)	Fwd	CGCGGATCCCATATGCAGCCGGATACGGTC	BamHI-NdeI
	Rev	CCCGCTCGAGAATCACTTCCAACACAAAAT	XhoI
NMB2050-(His/GST)	Fwd	CGCGGATCCCATATG-TGGTTGCTGATGAAGGGC	BamHI-NdeI
(MC58)	Rev	CCCGCTCGAG-GACTGCTTCATCTTCTGC	XhoI
NMB2050L	Fwd	CGCGGATCCCATATG-GAACTGATGACTGTTTTGC	NdeI
(MC58)	Rev	CCCGCTCGAG-TCAGACTGCTTCATCTTCT	XhoI
NMB2159-(His/GST)	Fwd	CGCGGATCCCATATG-AGCATTAAAGTAGCGATTAACGGTTTCGGC	BamHI-NdeI
(MC58)	Rev	CCCGCTCGAG-GATTTTGCCTGCGAAGTATTCCAAAGTGCG	XhoI
fu-ΔG287...-His	Fwd	CGCGGATCCGCTAGC-CCCGATGTTAAATCGGC	NheI

	Rev	CGGGGATCC-ATCCTGCTCTTTTTGCCGG	BamHI
fu-(ΔG287)-919-His	Fwd	CGCGGATCCGGTGGTGGTGGT-CAAAGCAAGAGCATCCAAACC	BamHI
	Rev	CCCAAGCTT-TTCGGGCGGTATTCGGGCTTC	HindIII
fu-(ΔG287)-953-His	Fwd	CGCGGATCCGGTGGTGGTGGT-GCCACCTACAAAGTGGAC	BamHI
	Rev	GCCCAAGCTT-TTGTTTGGCTGCCTCGAT	HindIII
fu-(ΔG287)-961-His	Fwd	CGCGGATCCGGTGGTGGTGGT-ACAAGCGACGACG	BamHI
	Rev	GCCCAAGCTT-CCACTCGTAATTGACGCC	HindIII
fu-(ΔG287)-Orf46.1-His	Fwd	CGCGGATCCGGTGGTGGTGGT-TCAGATTTGGCAAACGATTC	BamHI
	Rev	CCCAAGCTT-CGTATCATATTTCACGTGC	HindIII
fu-(ΔG287-919)-Orf46.1-His	Fwd	CCCAAGCTTGGTGGTGGTGGTGGT-TCAGATTTGGCAAACGATTC	HindIII
	Rev	CCCGCTCGAG-CGTATCATATTTCACGTGC	XhoI
fu-(ΔG287-Orf46.1)-919-His	Fwd	CCCAAGCTTGGTGGTGGTGGTGGT-CAAAGCAAGAGCATCCAAACC	HindIII
	Rev	CCCGCTCGAG-CGGGCGGTATTCGGGCTT	XhoI
fu ΔG287(394.98)-...	Fwd	CGCGGATCCGCTAGC-CCCGATGTTAAATCGGC	NheI
	Rev	CGGGGATCC-ATCCTGCTCTTTTTGCCGG	BamHI
fu Orf1-(Orf46.1)-His	Fwd	CGCGGATCCGCTAGC-GGACACACTTATTTCGGCATC	NheI
	Rev	CGCGGATCC-CCAGCGGTAGCCTAATTTGAT	
fu (Orf1)-Orf46.1-His	Fwd	CGCGGATCCGGTGGTGGTGGT-TCAGATTTGGCAAACGATTC	BamHI
	Rev	CCCAAGCTT-CGTATCATATTTCACGTGC	HindIII
fu (919)-Orf46.1-His	Fwd1	GCGGCGTCGACGGTGGCGGAGGCACTGGATCCTCAG	SalI
	Fwd2	GGAGGCACTGGATCCTCAGATTTGGCAAACGATTC	
	Rev	CCCGCTCGAG-CGTATCATATTTCACGTGC	XhoI
Fu orf46-....	Fwd	GGAATTCCATATGTCAGATTTGGCAAACGATTC	NdeI
	Rev	CGCGGATCCCGTATCATATTTCACGTGC	BamHI
Fu (orf46)-287-His	Fwd	CGGGGATCCGGGGGCGGCGGTGGCG	BamHI
	Rev	CCCAAGCTTATCCTGCTCTTTTTGCCGGC	HindIII
Fu (orf46)-919-His	Fwd	CGCGGATCCGGTGGTGGTGGTCAAAGCAAGAGCATCCAAACC	BamHI
	Rev	CCCAAGCTTCGGGCGGTATTCGGGCTTC	HindIII
Fu (orf46-919)-287-His	Fwd	CCCCAAGCTTGGGGGCGGCGGTGGCG	HindIII
	Rev	CCCGCTCGAGATCCTGCTCTTTTTGCCGGC	XhoI
Fu (orf46-287)-919-His	Fwd	CCCAAGCTTGGTGGTGGTGGTGGTCAAAGCAAGAGCATCCAAACC	HindIII
	Rev	CCCGCTCGAGCGGGCGGTATTCGGGCTT	XhoI
(ΔG741)-961c-His	Fwd1	GGAGGCACTGGATCCGCAGCCACAAACGACGACGA	XhoI
	Fwd2	GCGGCCTCGAG-GGTGGCGGAGGCACTGGATCCGCAG	
	Rev	CCCGCTCGAG-ACCCAGCTTGTAAGGTTG	XhoI
(ΔG741)-961-His	Fwd1	GGAGGCACTGGATCCGCAGCCACAAACGACGACGA	XhoI
	Fwd2	GCGGCCTCGAG-GGTGGCGGAGGCACTGGATCCGCAG	
	Rev	CCCGCTCGAG-CCACTCGTAATTGACGCC	XhoI

(ΔG741)-983-His	Fwd	GCGGCCTCGAG-GGATCCGGCGGAGGCGGCACTTCTGCG	XhoI
	Rev	CCCGCTCGAG-GAACCGGTAGCCTACG	XhoI
(ΔG741)-orf46.1-His	Fwd1 Fwd2	GGAGGCACTGGATCCTCAGATTTGGCAAACGATTC GCGGCGTCGACGGTGGCGGAGGCACTGGATCCTCAGA	SalI
	Rev	CCCGCTCGAG-CGTATCATATTTCACGTGC	XhoI
(ΔG983)-741(MC58) -His	Fwd	GCGGCCTCGAG-GGATCCGGAGGGGGTGGTGTCGCC	XhoI
	Rev	CCCGCTCGAG-TTGCTTGGCGGCAAG	XhoI
(ΔG983)-961c-His	Fwd1 Fwd2	GGAGGCACTGGATCCGCAGCCACAAACGACGACGA GCGGCCTCGAG-GGTGGCGGAGGCACTGGATCCGCAG	XhoI
	Rev	CCCGCTCGAG-ACCCAGCTTGTAAGGTTG	XhoI
(ΔG983)-961-His	Fwd1 Fwd2	GGAGGCACTGGATCCGCAGCCACAAACGACGACGA GCGGCCTCGAG-GGTGGCGGAGGCACTGGATCCGCAG	XhoI
	Rev	CCCGCTCGAG-CCACTCGTAATTGACGCC	XhoI
(ΔG983)- Orf46.1-His	Fwd1 Fwd2	GGAGGCACTGGATCCTCAGATTTGGCAAACGATTC GCGGCGTCGACGGTGGCGGAGGCACTGGATCCTCAGA	SalI
	Rev	CCCGCTCGAG-CGTATCATATTTCACGTGC	XhoI

* This primer was used as a Reverse primer for all the C terminal fusions of **287** to the His-tag.

§ Forward primers used in combination with the 287-His Reverse primer.

NB – All PCR reactions use strain 2996 unless otherwise specified (*e.g.* strain MC58)

[0293] In all constructs starting with an ATG not followed by a unique *Nhe*I site, the ATG codon is part of the *Nde*I site used for cloning. The constructs made using *Nhe*I as a cloning site at the 5' end (e.g. all those containing 287 at the N-terminus) have two additional codons (GCT AGC) fused to the coding sequence of the antigen.

Preparation of chromosomal DNA templates

[0294] *N.meningitidis* strains 2996, MC58, 394.98, 1000 and BZ232 (and others) were grown to exponential phase in 100ml of GC medium, harvested by centrifugation, and resuspended in 5ml buffer (20% w/v sucrose, 50mM Tris-HCl, 50mM EDTA, pH8). After 10 minutes incubation on ice, the bacteria were lysed by adding 10ml of lysis solution (50mM NaCl, 1% Na-Sarkosyl, 50μg/ml Proteinase K), and the suspension incubated at 37°C for 2 hours. Two phenol extractions (equilibrated to pH 8) and one $CHCl_3$/isoamylalcohol (24:1) extraction were performed. DNA was precipitated by addition of 0.3M sodium acetate and 2 volumes of ethanol, and collected by centrifugation. The pellet was washed once with 70%(v/v) ethanol and redissolved in 4.0ml TE buffer (10mM Tris-HCl, 1mM EDTA, pH 8.0). The DNA concentration was measured by reading OD_{260}.

PCR Amplification

[0295] The standard PCR protocol was as follows: 200ng of genomic DNA from 2996, MC581000, or BZ232 strains or 10ng of plasmid DNA preparation of recombinant clones were used as template in the presence of 40μM of each oligonucletide primer, 400-800 μM dNTPs solution, 1x PCR buffer (including 1.5mM $MgCl_2$), 2.5 units *TaqI* DNA polymerase (using Perkin-Elmer AmpliTaQ, Boerhingher Mannheim Expand™ Long Template).

[0296] After a preliminary 3 minute incubation of the whole mix at 95°C, each sample underwent a two-step amplification: the first 5 cycles were performed using the hybridisation temperature that excluded the restriction enzyme tail of the primer (T_{m1}). This was followed by 30 cycles according to the hybridisation temperature calculated for the whole length oligos (T_{m2}). Elongation times, performed at 68°C or 72°C, varied according to the length of the Orf to be amplified. In the case of Orf1 the elongation time, starting from 3 minutes, was increased by 15 seconds each cycle. The cycles were completed with a 10 minute extension step at 72°C.

[0297] The amplified DNA was either loaded directly on a 1% agarose gel. The DNA fragment corresponding to the band of correct size was purified from the gel using the Qiagen Gel Extraction Kit, following the manufacturer's protocol.

Digestion of PCR fragments and of the cloning vectors

[0298] The purified DNA corresponding to the amplified fragment was digested with the appropriate restriction enzymes for cloning into pET-21b+, pET22b+ or pET-24b+. Digested fragments were purified using the QIAquick PCR purification kit (following the manufacturer's instructions) and eluted with either H_2O or 10mM Tris, pH 8.5. Plasmid vectors were digested with the appropriate restriction enzymes, loaded onto a 1.0% agarose gel and the band corresponding to the digested vector purified using the Qiagen QIAquick Gel Extraction Kit.

Cloning

[0299] The fragments corresponding to each gene, previously digested and purified, were ligated into pET21 b+, pET22b+ or pET-24b+. A molar ratio of 3:1 fragment/vector was used with T4 DNA ligase in the ligation buffer supplied by the manufacturer.

[0300] Recombinant plasmid was transformed into competent *E.coli* DH5 or HB101 by incubating the ligase reaction solution and bacteria for 40 minutes on ice, then at 37°C for 3 minutes.

[0301] This was followed by the addition of 800μl LB broth and incubation at 37°C for 20 minutes. The cells were centrifuged at maximum speed in an Eppendorf microfuge, resuspended in approximately 200μl of the supernatant and plated onto LB ampicillin (100mg/ml) agar.

[0302] Screening for recombinant clones was performed by growing randomly selected colonies overnight at 37°C in 4.0ml of LB broth + 100μg/ml ampicillin. Cells were pelleted and plasmid DNA extracted using the Qiagen QIAprep Spin Miniprep Kit, following the manufacturer's instructions. Approximately 1μg of each individual miniprep was digested with the appropriate restriction enzymes and the digest loaded onto a 1-1.5% agarose gel (depending on the expected insert size), in parallel with the molecular weight marker (1kb DNA Ladder, GIBCO). Positive clones were selected on the basis of the size of insert.

Expression

[0303] After cloning each gene into the expression vector, recombinant plasmids were transformed into *E.coli* strains suitable for expression of the recombinant protein. 1μl of each construct was used to transform *E.coli* BL21-DE3 as described above. Single recombinant colonies were inoculated into 2ml LB+Amp (100μg/ml), incubated at 37°C overnight, then diluted 1:30 in 20ml of LB+Amp (100μg/ml) in 100ml flasks, to give an OD_{600} between 0.1 and 0.2. The flasks were incubated at 30°C or at 37°C in a gyratory water bath shaker until OD_{600} indicated exponential growth suitable for induction of expression (0.4-0.8 OD). Protein expression was induced by addition of 1.0mM IPTG. After 3 hours incubation at 30°C or 37°C the OD_{600} was measured and expression examined. 1.0ml of each sample was centrifuged in a microfuge, the pellet resuspended in PBS and analysed by SDS-PAGE and Coomassie Blue staining.

Gateway cloning and expression

[0304] Sequences labelled GATE were cloned and expressed using the GATEWAY Cloning Technology (GIBCO-BRL). Recombinational cloning (RC) is based on the recombination reactions that mediate the integration and excision of phage into and from the *E.coli* genome, respectively. The integration involves recombination of the *attP* site of the phage DNA within the *attB* site located in the bacterial genome (BP reaction) and generates an integrated phage genome flanked by *attL* and *attR* sites. The excision recombines *attL* and *attR* sites back to *attP* and *attB* sites (LR reaction). The integration reaction requires two enzymes [the phage protein Integrase (Int) and the bacterial protein integration host factor (IHF)] (BP clonase). The excision reaction requires Int, IHF, and an additional phage enzyme, Excisionase (Xis) (LR clonase). Artificial derivatives of the 25-bp bacterial *attB* recombination site, referred to as B 1 and B2, were added to the 5' end of the primers used in PCR reactions to amplify Neisserial ORFs. The resulting products were BP cloned into a "Donor vector" containing complementary derivatives of the phage *attP* recombination site (P1 and P2) using BP clonase. The resulting "Entry clones" contain ORFs flanked by derivatives of the *attL* site (Ll and L2) and were subcloned into expression "destination vectors" which contain derivatives of the *attL*-compatible *attR* sites (R1 and R2) using LR clonase. This resulted in "expression clones" in which ORFs are flanked by B1 and B2 and fused in frame to the GST or His N terminal tags.

[0305] The *E. coli* strain used for GATEWAY expression is BL21-SI. Cells of this strain are induced for expression of the T7 RNA polymerase by growth in medium containing salt (0.3 M NaCl).

[0306] Note that this system gives N-terminus His tags.

Preparation of membrane proteins.

[0307] Fractions composed principally of either inner, outer or total membrane were isolated in order to obtain recombinant proteins expressed with membrane-localisation leader sequences. The method for preparation of membrane fractions, enriched for recombinant proteins, was adapted from Filip et. al. [J.Bact. (1973) 115:717-722] and Davies et. al. [J.Immunol.Meth. (1990) 143:215-225]. Single colonies harbouring the plasmid of interest were grown overnight at 37°C in 20 ml of LB/Amp (100 μg/ml) liquid culture. Bacteria were diluted 1:30 in 1.0 L of fresh medium and grown at either 30°C or 37°C until the OD_{550} reached 0.6-0.8. Expression of recombinant protein was induced with IPTG at a final concentration of 1.0 mM. After incubation for 3 hours, bacteria were harvested by centrifugation at 8000*g* for 15 minutes at 4°C and resuspended in 20 ml of 20 mM Tris-HCl (pH 7.5) and complete protease inhibitors (Boehringer-Mannheim). All subsequent procedures were performed at 4°C or on ice.

[0308] Cells were disrupted by sonication using a Branson Sonifier 450 and centrifuged at 5000g for 20 min to sediment unbroken cells and inclusion bodies. The supernatant, containing membranes and cellular debris, was centrifuged at 50000g (Beckman Ti50, 29000rpm) for 75 min, washed with 20 mM Bis-tris propane (pH 6.5), 1.0 M NaCl, 10% (v/v) glycerol and sedimented again at 50000g for 75 minutes. The pellet was resuspended in 20mM Tris-HCl (pH 7.5), 2.0% (v/v) Sarkosyl, complete protease inhibitor (1.0 mM EDTA, final concentration) and incubated for 20 minutes to dissolve inner membrane. Cellular debris was pelleted by centrifugation at 5000g for 10 min and the supernatant centrifuged at 75000g for 75 minutes (Beckman Ti50, 33000rpm). Proteins 008L and 519L were found in the supernatant suggesting inner membrane localisation. For these proteins both inner and total membrane fractions (washed with NaCl as above) were used to immunise mice. Outer membrane vesicles obtained from the 75000g pellet were washed with 20 mM Tris-HCl (pH 7.5) and centrifuged at 75000g for 75 minutes or overnight. The OMV was finally resuspended in 500 μl of 20 mM Tris-HCl (pH 7.5), 10% v/v glycerol. Orf1L and Orf40L were both localised and enriched in the outer membrane fraction which was used to immunise mice. Protein concentration was estimated by standard Bradford Assay (Bio-Rad), while protein concentration of inner membrane fraction was determined with the DC protein assay (Bio-Rad). Various fractions from the isolation procedure were assayed by SDS-PAGE.

Purification of His-tagged proteins

[0309] Various forms of 287 were cloned from strains 2996 and MC58. They were constructed with a C-terminus His-tagged fusion and included a mature form (aa 18-427), constructs with deletions (Δ1, Δ 2, Δ3 and Δ4) and clones composed of either B or C domains. For each clone purified as a His-fusion, a single colony was streaked and grown overnight at 37°C on a LB/Amp (100 μg/ml) agar plate. An isolated colony from this plate was inoculated into 20ml of LB/Amp (100 μg/ml) liquid medium and grown overnight at 37°C with shaking. The overnight culture was diluted 1:30 into 1.0 L LB/Amp (100 μg/ml) liquid medium and allowed to grow at the optimal temperature (30 or 37°C) until the OD_{550} reached 0.6-0.8. Expression of recombinant protein was induced by addition of IPTG (final concentration 1.0mM) and the culture incubated for a further 3 hours. Bacteria were harvested by centrifugation at 8000g for 15 min at 4°C. The bacterial pellet was resuspended in 7.5 ml of either (i) cold buffer A (300 mM NaCl, 50 mM phosphate buffer, 10 mM imidazole, pH 8.0) for soluble proteins or (ii) buffer B (10mM Tris-HCl, 100 mM phosphate buffer, pH 8.8 and, optionally, 8M urea) for insoluble proteins. Proteins purified in a soluble form included 287-His, Δ1, Δ2, Δ3 and Δ4287-His, Δ4287MC58-His, 287c-His and 287cMC58-His. Protein 287bMC58-His was insoluble and purified accordingly. Cells were disrupted by sonication on ice four times for 30 sec at 40W using a Branson sonifier 450 and centrifuged at 13000xg for 30 min at 4°C. For insoluble proteins, pellets were resuspended in 2.0 ml buffer C (6 M guanidine hydrochloride, 100 mM phosphate buffer, 10 mM Tris- HCl, pH 7.5 and treated with 10 passes of a Dounce homogenizer. The homogenate was centrifuged at 13000g for 30 min and the supernatant retained. Supernatants for both soluble and insoluble preparations were mixed with 150μl Ni^{2+}-resin (previously equilibrated with either buffer A or buffer B, as appropriate) and incubated at room temperature with gentle agitation for 30 min. The resin was Chelating Sepharose Fast Flow (Pharmacia), prepared according to the manufacturer's protocol. The batch-wise preparation was centrifuged at 700g for 5 min at 4°C and the supernatant discarded. The resin was washed twice (batch-wise) with 10ml buffer A or B for 10 min, resuspended in 1.0 ml buffer A or B and loaded onto a disposable column. The resin continued to be washed with either (i) buffer A at 4°C or (ii) buffer B at room temperature, until the OD_{280} of the flow-through reached 0.02-0.01. The resin was further washed with either (i) cold buffer C (300mM NaCl, 50mM phosphate buffer, 20mM imidazole, pH 8.0) or (ii) buffer D (10mM Tris-HCl, 100mM phosphate buffer, pH 6.3 and, optionally, 8M urea) until OD_{280} of the flow-through reached 0.02-0.01. The His-fusion protein was eluted by addition of 700μl of either (i) cold elution buffer A (300 mM NaCl, 50mM phosphate buffer, 250 mM imidazole, pH 8.0) or (ii) elution buffer B (10 mM Tris-HCl, 100 mM phosphate buffer, pH 4.5 and, optionally, 8M urea) and fractions collected until the OD_{280} indicated all the recombinant protein was obtained. 20μl aliquots of each elution fraction were analysed by SDS-PAGE. Protein concentrations were estimated using the Bradford assay.

Renaturation of denatured His-fusion proteins.

[0310] Denaturation was required to solubilize 287bMC8, so a renaturation step was employed prior to immunisation. Glycerol was added to the denatured fractions obtained above to give a final concentration of 10% v/v. The proteins were diluted to 200 μg/ml using dialysis buffer I (10% v/v glycerol, 0.5M arginine, 50 mM phosphate buffer, 5.0 mM reduced glutathione, 0.5 mM oxidised glutathione, 2.0M urea, pH 8.8) and dialysed against the same buffer for 12-14 hours at 4°C. Further dialysis was performed with buffer II (10% v/v glycerol, 0.5M arginine, 50mM phosphate buffer, 5.0mM reduced glutathione, 0.5mM oxidised glutathione, pH 8.8) for 12-14 hours at 4°C. Protein concentration was estimated using the formula:

$$Protein\ (mg/ml) = (1.55 \times OD_{280}) - (0.76 \times OD_{260})$$

Amino acid sequence analysis.

[0311] Automated sequence analysis of the NH_2-terminus of proteins was performed on a Beckman sequencer (LF 3000) equipped with an on-line phenylthiohydantoin-amino acid analyser (System Gold) according to the manufacturer's recommendations.

Immunization

[0312] Balb/C mice were immunized with antigens on days 0, 21 and 35 and sera analyzed at day 49.

Sera analysis - ELISA

[0313] The acapsulated MenB M7 and the capsulated strains were plated on chocolate agar plates and incubated overnight at 37°C with 5% CO_2. Bacterial colonies were collected from the agar plates using a sterile dracon swab and inoculated into Mueller-Hinton Broth (Difco) containing 0.25% glucose. Bacterial growth was monitored every 30 minutes by following OD_{620}. The bacteria were let to grow until the OD reached the value of 0.4-0.5. The culture was centrifuged for 10 minutes at 4000rpm. The supernatant was discarded and bacteria were washed twice with PBS, resuspended in PBS containing 0.025% formaldehyde, and incubated for 1 hour at 37°C and then overnight at 4°C with stirring. 100μl bacterial cells were added to each well of a 96 well Greiner plate and incubated overnight at 4°C. The wells were then washed three times with PBT washing buffer (0.1% Tween-20 in PBS). 200μl of saturation buffer (2.7% polyvinylpyrrolidone 10 in water) was added to each well and the plates incubated for 2 hours at 37°C. Wells were washed three times with PBT. 200μl of diluted sera (Dilution buffer: 1% BSA, 0.1 % Tween-20, 0.1 % NaN_3 in PBS) were added to each well and the plates incubated for 2 hours at 37°C. Wells were washed three times with PBT. 100μl of HRP-conjugated rabbit anti-mouse (Dako) serum diluted 1:2000 in dilution buffer were added to each well and the plates were incubated for 90 minutes at 37°C. Wells were washed three times with PBT buffer. 100μl of substrate buffer for HRP (25ml of citrate buffer pH5, 10mg of O-phenildiamine and 10μl of H_2O_2) were added to each well and the plates were left at room temperature for 20 minutes. 100μl 12.5% H_2SO_4 was added to each well and OD_{490} was followed. The ELISA titers were calculated abitrarely as the dilution of sera which gave an OD_{490} value of 0.4 above the level of preimmune sera. The ELISA was considered positive when the dilution of sera with OD_{490} of 0.4 was higher than 1:400.

Sera analysis - FACS Scan bacteria binding assay

[0314] The acapsulated MenB M7 strain was plated on chocolate agar plates and incubated overnight at 37°C with 5% CO_2. Bacterial colonies were collected from the agar plates using a sterile dracon swab and inoculated into 4 tubes containing 8ml each Mueller-Hinton Broth (Difco) containing 0.25% glucose. Bacterial growth was monitored every 30 minutes by following OD_{620}. The bacteria were let to grow until the OD reached the value of 0.35-0.5. The culture was centrifuged for 10 minutes at 4000rpm. The supernatant was discarded and the pellet was resuspended in blocking buffer (1% BSA in PBS, 0.4% NaN_3) and centrifuged for 5 minutes at 4000rpm. Cells were resuspended in blocking buffer to reach OD_{620} of 0.05. 100μl bacterial cells were added to each well of a Costar 96 well plate. 100μl of diluted (1:100, 1:200, 1:400) sera (in blocking buffer) were added to each well and plates incubated for 2 hours at 4°C. Cells were centrifuged for 5 minutes at 4000rpm, the supernatant aspirated and cells washed by addition of 200μl/well of blocking buffer in each well. 100μl of R-Phicoerytrin conjugated $F(ab)_2$ goat anti-mouse, diluted 1:100, was added to each well and plates incubated for 1 hour at 4°C. Cells were spun down by centrifugation at 4000rpm for 5 minutes and washed by addition of 200μl/well of blocking buffer. The supernatant was aspirated and cells resuspended in 200μl/

well of PBS, 0.25% formaldehyde. Samples were transferred to FACScan tubes and read. The condition for FACScan (Laser Power 15mW) setting were: FL2 on; FSC-H threshold:92; FSC PMT Voltage: E 01; SSC PMT: 474; Amp. Gains 6.1; FL-2 PMT: 586; compensation values: 0.

Sera analysis - bactericidal assay

[0315] *N. meningitidis* strain 2996 was grown overnight at 37°C on chocolate agar plates (starting from a frozen stock) with 5% CO_2. Colonies were collected and used to inoculate 7ml Mueller-Hinton broth, containing 0.25% glucose to reach an OD_{620} of 0.05-0.08. The culture was incubated for approximately 1.5 hours at 37 degrees with shacking until the OD_{620} reached the value of 0.23-0.24. Bacteria were diluted in 50mM Phosphate buffer pH 7.2 containing 10mM $MgCl_2$, 10mM $CaCl_2$ and 0.5% (w/v) BSA (assay buffer) at the working dilution of 10^5 CFU/ml. The total volume of the final reaction mixture was 50 μl with 25 μl of serial two fold dilution of test serum, 12.5 μl of bacteria at the working dilution, 12.5 μl of baby rabbit complement (final concentration 25%).

[0316] Controls included bacteria incubated with complement serum, immune sera incubated with bacteria and with complement inactivated by heating at 56°C for 30'. Immediately after the addition of the baby rabbit complement, 10μl of the controls were plated on Mueller-Hinton agar plates using the tilt method (time 0). The 96-wells plate was incubated for 1 hour at 37°C with rotation. 7μl of each sample were plated on Mueller-Hinton agar plates as spots, whereas 10μl of the controls were plated on Mueller-Hinton agar plates using the tilt method (time 1). Agar plates were incubated for 18 hours at 37 degrees and the colonies corresponding to time 0 and time 1 were counted.

Sera analysis - western blots

[0317] Purified proteins (500ng/lane), outer membrane vesicles (5μg) and total cell extracts (25μg) derived from MenB strain 2996 were loaded onto a 12% SDS-polyacrylamide gel and transferred to a nitrocellulose membrane. The transfer was performed for 2 hours at 150mA at 4°C, using transfer buffer (0.3% Tris base, 1.44% glycine, 20% (v/v) methanol). The membrane was saturated by overnight incubation at 4°C in saturation buffer (10% skimmed milk, 0.1% Triton X100 in PBS). The membrane was washed twice with washing buffer (3% skimmed milk, 0.1% Triton X100 in PBS) and incubated for 2 hours at 37°C with mice sera diluted 1:200 in washing buffer. The membrane was washed twice and incubated for 90 minutes with a 1:2000 dilution of horseradish peroxidase labelled anti-mouse Ig. The membrane was washed twice with 0.1% Triton X100 in PBS and developed with the Opti-4CN Substrate Kit (Bio-Rad). The reaction was stopped by adding water.

[0318] The OMVs were prepared as follows: *N. meningitidis* strain 2996 was grown overnight at 37 degrees with 5% CO_2 on 5 GC plates, harvested with a loop and resuspended in 10 ml of 20mM Tris-HCl pH 7.5, 2 mM EDTA. Heat inactivation was performed at 56°C for 45 minutes and the bacteria disrupted by sonication for 5 minutes on ice (50% duty cycle, 50% output, Branson sonifier 3 mm microtip). Unbroken cells were removed by centrifugation at 5000g for 10 minutes, the supernatant containing the total cell envelope fraction recovered and further centrifuged overnight at 50000g at the temperature of 4°C . The pellet containing the membranes was resuspended in 2% sarkosyl, 20mM Tris-HCl pH 7.5, 2 mM EDTA and incubated at room temperature for 20 minutes to solubilise the inner membranes. The suspension was centrifuged at 10000g for 10 minutes to remove aggregates, the supernatant was further centrifuged at 50000g for 3 hours. The pellet, containing the outer membranes was washed in PBS and resuspended in the same buffer. Protein concentration was measured by the D.C. Bio-Rad Protein assay (Modified Lowry method), using BSA as a standard.

[0319] Total cell extracts were prepared as follows: *N. meningitidis* strain 2996 was grown overnight on a GC plate, harvested with a loop and resuspended in 1ml of 20mM Tris-HCl. Heat inactivation was performed at 56°C for 30 minutes.

961 domain studies

[0320] Cellular fractions preparation Total lysate, periplasm, supernatant and OMV of *E.coli* clones expressing different domains of 961 were prepared using bacteria from over-night cultures or after 3 hours induction with IPTG. Briefly, the periplasm were obtained suspending bacteria in saccarose 25% and Tris 50mM (pH 8) with polimixine 100μg/ml. After 1hr at room temperature bacteria were centrifuged at 13000rpm for 15 min and the supernatant were collected. The culture supernatant were filtered with 0.2μm and precipitated with TCA 50% in ice for two hours. After centrifugation (30 min at 13000 rp) pellets were rinsed twice with ethanol 70% and suspended in PBS. The OMV preparation was performed as previously described. Each cellular fraction were analyzed in SDS-PAGE or in Western Blot using the polyclonal anti-serum raised against GST-961.

[0321] Adhesion assay Chang epithelial cells (Wong-Kilbourne derivative, clone 1-5c-4, human conjunctiva) were maintained in DMEM (Gibco) supplemented with 10% heat-inactivated FCS, 15mM L-glutamine and antibiotics.

[0322] For the adherence assay, sub-confluent culture of Chang epithelial cells were rinsed with PBS and treated with

trypsin-EDTA (Gibco), to release them from the plastic support. The cells were then suspended in PBS, counted and dilute in PBS to $5x10^5$ cells/ml.

[0323] Bacteria from over-night cultures or after induction with IPTG, were pelleted and washed twice with PBS by centrifuging at 13000 for 5 min. Approximately $2\text{-}3x10^8$ (cfu) were incubated with 0.5 mg/ml FITC (Sigma) in 1ml buffer containing 50mM $NaHCO_3$ and 100mM NaCl pH 8, for 30 min at room temperature in the dark. FITC-labeled bacteria were wash 2-3 times and suspended in PBS at $1\text{-}1.5x10^9$/ml. 200μl of this suspension ($2\text{-}3x10^8$) were incubated with 200μl ($1x10^5$) epithelial cells for 30min a 37°C. Cells were than centrifuged at 2000rpm for 5 min to remove non-adherent bacteria, suspended in 200μl of PBS, transferred to FACScan tubes and read

Annex to the application documents - subsequently filed sequences listing

[0324]

SEQUENCE LISTING

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<223> Oligonucleotide

<400> 28
ccggaattct tatgtcagat ttggcaaacg attctt 36

<210> 29
<211> 35
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 29
gcccaagctt ttacgtatca tatttcacgt gcttc 35

<210> 30
<211> 37
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 30
ccggaattct tatgtcgccc gatgttaaat cggcgga 37

<210> 31
<211> 35
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 31
gcccaagctt ttacgtatca tatttcacgt gcttc 35

<210> 32
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
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<400> 32
ccggaattct tatgcaaagc aagagcatcc aaacct 36

<210> 33
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 33
gcccaagctt ttacgggcgg tattcgggct 30

<210> 34
<211> 29
<212> DNA

<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 34
ccggaattca tatgaaacac tttccatcc 29

<210> 35
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<223> Oligonucleotide

<400> 35
gcccaagctt ttaccactcg taattgac 28

<210> 36
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<400> 36
ccggaattca tatggccaca agcgacgac 29

<210> 37
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<400> 37
gcccaagctt ttaccactcg taattgac 28

<210> 38
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<400> 38
ccggaattct tatgaaacac tttccatcc 29

<210> 39
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<400> 39
gcccaagctt tcaacccacg ttgtaaggtt g 31

<210> 40
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<220>

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<400> 40
ccggaattct tatggccaca aacgacgacg 30

<210> 41
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<212> DNA
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<220>
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<400> 41
gcccaagctt tcaacccacg ttgtaaggtt g 31

<210> 42
<211> 34
<212> DNA
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<220>
<223> Oligonucleotide

<400> 42
ccggaattct tatggccacc tacaaagtgg acga 34

<210> 43
<211> 32
<212> DNA
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<220>
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<400> 43
gcccaagctt ttattgtttg gctgcctcga tt 32

<210> 44
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<212> DNA
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<220>
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<400> 44
cgcggatccg ctagccccga tgttaaatcg gc 32

<210> 45
<211> 31
<212> DNA
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<220>
<223> Oligonucleotide

<400> 45
cccgctcgag tcaatcctgc tctttttgc c 31

<210> 46
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<212> DNA
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<400> 46

cgcggatccg ctagccaaga tatggcggca gt 32

<210> 47
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<220>
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<400> 47
cgcggatccg ctagcgccga atccgcaaat ca 32

<210> 48
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<212> DNA
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<220>
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<400> 48
cgcgctagcg gaagggttga tttggctaat gg 32

<210> 49
<211> 34
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 49
gggaattcca tatgggcatt tcccgcaaaa tatc 34

<210> 50
<211> 32
<212> DNA
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<220>
<223> Oligonucleotide

<400> 50
cccgctcgag ttacgtatca tatttcacgt gc 32

<210> 51
<211> 34
<212> DNA
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<220>
<223> Oligonucleotide

<400> 51
gggaattcca tatgggcatt tcccgcaaaa tatc 34

<210> 52
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<212> DNA
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<220>
<223> Oligonucleotide

<400> 52
cccgctcgag ttattctatg ccttgtgcgg cat 33

<210> 53

<211> 32
<212> DNA
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<220>
<223> Oligonucleotide

<400> 53
cgcggatccc atatggccac aagcgacgac ga 32

<210> 54
<211> 28
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<220>
<223> Oligonucleotide

<400> 54
cccgctcgag ttaccactcg taattgac 28

<210> 55
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 55
cgcggatccc atatggccac aaacgacg 28

<210> 56
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<212> DNA
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<220>
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<400> 56
cccgctcgag tcatttagca atattatctt tgttc 35

<210> 57
<211> 33
<212> DNA
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<220>
<223> Oligonucleotide

<400> 57
cgcggatccc atatgaaagc aaacagtgcc gac 33

<210> 58
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 58
cccgctcgag ttaccactcg taattgac 28

<210> 59
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 59
cgcggatccc atatggccac aaacgacg 28

<210> 60
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 60
cccgctcgag ttaacccacg ttgtaaggt 29

<210> 61
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 61
cgcggatccc atatgatgaa acactttcca tcc 33

<210> 62
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 62
cccgctcgag ttaacccacg ttgtaaggt 29

<210> 63
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 63
cgcggatccc atatggccac aaacgacg 28

<210> 64
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<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 64
cccgctcgag tcagtctgac actgttttat cc 32

<210> 65
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 65
cgcggatccg ctagccccga tgttaaatcg gc 32

<210> 66
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 66
cccgctcgag ttacgggcgg tattcgg 27

<210> 67
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 67
cgcggatccg ctagccccga tgttaaatcg gc 32

<210> 68
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 68
cccgctcgag ttacgtatca tatttcacgt gc 32

<210> 69
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 69
cgcggatccg ctagccccga tgttaaatcg gc 32

<210> 70
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 70
cccgctcgag ttaccactcg taattgac 28

<210> 71
<211> 1457
<212> PRT
<213> Neisseria meningitidis

<400> 71
Met Lys Thr Thr Asp Lys Arg Thr Thr Glu Thr His Arg Lys Ala Pro
1 5 10 15

Lys Thr Gly Arg Ile Arg Phe Ser Pro Ala Tyr Leu Ala Ile Cys Leu

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                20                  25                  30
Ser Phe Gly Ile Leu Pro Gln Ala Trp Ala Gly His Thr Tyr Phe Gly
        35                  40                  45
Ile Asn Tyr Gln Tyr Tyr Arg Asp Phe Ala Glu Asn Lys Gly Lys Phe
    50                  55                  60
Ala Val Gly Ala Lys Asp Ile Glu Val Tyr Asn Lys Lys Gly Glu Leu
65                  70                  75                  80
Val Gly Lys Ser Met Thr Lys Ala Pro Met Ile Asp Phe Ser Val Val
                85                  90                  95
Ser Arg Asn Gly Val Ala Ala Leu Val Gly Asp Gln Tyr Ile Val Ser
            100                 105                 110
Val Ala His Asn Gly Gly Tyr Asn Asn Val Asp Phe Gly Ala Glu Gly
        115                 120                 125
Arg Asn Pro Asp Gln His Arg Phe Thr Tyr Lys Ile Val Lys Arg Asn
    130                 135                 140
Asn Tyr Lys Ala Gly Thr Lys Gly His Pro Tyr Gly Gly Asp Tyr His
145                 150                 155                 160
Met Pro Arg Leu His Lys Phe Val Thr Asp Ala Glu Pro Val Glu Met
                165                 170                 175
Thr Ser Tyr Met Asp Gly Arg Lys Tyr Ile Asp Gln Asn Asn Tyr Pro
            180                 185                 190
Asp Arg Val Arg Ile Gly Ala Gly Arg Gln Tyr Trp Arg Ser Asp Glu
        195                 200                 205
Asp Glu Pro Asn Asn Arg Glu Ser Ser Tyr His Ile Ala Ser Ala Tyr
    210                 215                 220
Ser Trp Leu Val Gly Gly Asn Thr Phe Ala Gln Asn Gly Ser Gly Gly
225                 230                 235                 240
Gly Thr Val Asn Leu Gly Ser Glu Lys Ile Lys His Ser Pro Tyr Gly
                245                 250                 255
Phe Leu Pro Thr Gly Gly Ser Phe Gly Asp Ser Gly Ser Pro Met Phe
            260                 265                 270
Ile Tyr Asp Ala Gln Lys Gln Lys Trp Leu Ile Asn Gly Val Leu Gln
        275                 280                 285
Thr Gly Asn Pro Tyr Ile Gly Lys Ser Asn Gly Phe Gln Leu Val Arg
    290                 295                 300
Lys Asp Trp Phe Tyr Asp Glu Ile Phe Ala Gly Asp Thr His Ser Val
305                 310                 315                 320
Phe Tyr Glu Pro Arg Gln Asn Gly Lys Tyr Ser Phe Asn Asp Asp Asn
                325                 330                 335
Asn Gly Thr Gly Lys Ile Asn Ala Lys His Glu His Asn Ser Leu Pro
            340                 345                 350
Asn Arg Leu Lys Thr Arg Thr Val Gln Leu Phe Asn Val Ser Leu Ser
        355                 360                 365
Glu Thr Ala Arg Glu Pro Val Tyr His Ala Ala Gly Gly Val Asn Ser
    370                 375                 380
Tyr Arg Pro Arg Leu Asn Asn Gly Glu Asn Ile Ser Phe Ile Asp Glu
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385 390 395 400

Gly Lys Gly Glu Leu Ile Leu Thr Ser Asn Ile Asn Gln Gly Ala Gly
405 410 415

Gly Leu Tyr Phe Gln Gly Asp Phe Thr Val Ser Pro Glu Asn Asn Glu
420 425 430

Thr Trp Gln Gly Ala Gly Val His Ile Ser Glu Asp Ser Thr Val Thr
435 440 445

Trp Lys Val Asn Gly Val Ala Asn Asp Arg Leu Ser Lys Ile Gly Lys
450 455 460

Gly Thr Leu His Val Gln Ala Lys Gly Glu Asn Gln Gly Ser Ile Ser
465 470 475 480

Val Gly Asp Gly Thr Val Ile Leu Asp Gln Gln Ala Asp Asp Lys Gly
485 490 495

Lys Lys Gln Ala Phe Ser Glu Ile Gly Leu Val Ser Gly Arg Gly Thr
500 505 510

Val Gln Leu Asn Ala Asp Asn Gln Phe Asn Pro Asp Lys Leu Tyr Phe
515 520 525

Gly Phe Arg Gly Gly Arg Leu Asp Leu Asn Gly His Ser Leu Ser Phe
530 535 540

His Arg Ile Gln Asn Thr Asp Glu Gly Ala Met Ile Val Asn His Asn
545 550 555 560

Gln Asp Lys Glu Ser Thr Val Thr Ile Thr Gly Asn Lys Asp Ile Ala
565 570 575

Thr Thr Gly Asn Asn Asn Ser Leu Asp Ser Lys Lys Glu Ile Ala Tyr
580 585 590

Asn Gly Trp Phe Gly Glu Lys Asp Thr Thr Lys Thr Asn Gly Arg Leu
595 600 605

Asn Leu Val Tyr Gln Pro Ala Ala Glu Asp Arg Thr Leu Leu Leu Ser
610 615 620

Gly Gly Thr Asn Leu Asn Gly Asn Ile Thr Gln Thr Asn Gly Lys Leu
625 630 635 640

Phe Phe Ser Gly Arg Pro Thr Pro His Ala Tyr Asn His Leu Asn Asp
645 650 655

His Trp Ser Gln Lys Glu Gly Ile Pro Arg Gly Glu Ile Val Trp Asp
660 665 670

Asn Asp Trp Ile Asn Arg Thr Phe Lys Ala Glu Asn Phe Gln Ile Lys
675 680 685

Gly Gly Gln Ala Val Val Ser Arg Asn Val Ala Lys Val Lys Gly Asp
690 695 700

Trp His Leu Ser Asn His Ala Gln Ala Val Phe Gly Val Ala Pro His
705 710 715 720

Gln Ser His Thr Ile Cys Thr Arg Ser Asp Trp Thr Gly Leu Thr Asn
725 730 735

Cys Val Glu Lys Thr Ile Thr Asp Asp Lys Val Ile Ala Ser Leu Thr
740 745 750

Lys Thr Asp Ile Ser Gly Asn Val Asp Leu Ala Asp His Ala His Leu

755 760 765

Asn Leu Thr Gly Leu Ala Thr Leu Asn Gly Asn Leu Ser Ala Asn Gly
770 775 780

Asp Thr Arg Tyr Thr Val Ser His Asn Ala Thr Gln Asn Gly Asn Leu
785 790 795 800

Ser Leu Val Gly Asn Ala Gln Ala Thr Phe Asn Gln Ala Thr Leu Asn
805 810 815

Gly Asn Thr Ser Ala Ser Gly Asn Ala Ser Phe Asn Leu Ser Asp His
820 825 830

Ala Val Gln Asn Gly Ser Leu Thr Leu Ser Gly Asn Ala Lys Ala Asn
835 840 845

Val Ser His Ser Ala Leu Asn Gly Asn Val Ser Leu Ala Asp Lys Ala
850 855 860

Val Phe His Phe Glu Ser Ser Arg Phe Thr Gly Gln Ile Ser Gly Gly
865 870 875 880

Lys Asp Thr Ala Leu His Leu Lys Asp Ser Glu Trp Thr Leu Pro Ser
885 890 895

Gly Thr Glu Leu Gly Asn Leu Asn Leu Asp Asn Ala Thr Ile Thr Leu
900 905 910

Asn Ser Ala Tyr Arg His Asp Ala Ala Gly Ala Gln Thr Gly Ser Ala
915 920 925

Thr Asp Ala Pro Arg Arg Arg Ser Arg Arg Ser Arg Arg Ser Leu Leu
930 935 940

Ser Val Thr Pro Pro Thr Ser Val Glu Ser Arg Phe Asn Thr Leu Thr
945 950 955 960

Val Asn Gly Lys Leu Asn Gly Gln Gly Thr Phe Arg Phe Met Ser Glu
965 970 975

Leu Phe Gly Tyr Arg Ser Asp Lys Leu Lys Leu Ala Glu Ser Ser Glu
980 985 990

Gly Thr Tyr Thr Leu Ala Val Asn Asn Thr Gly Asn Glu Pro Ala Ser
995 1000 1005

Leu Glu Gln Leu Thr Val Val Glu Gly Lys Asp Asn Lys Pro Leu Ser
1010 1015 1020

Glu Asn Leu Asn Phe Thr Leu Gln Asn Glu His Val Asp Ala Gly Ala
1025 1030 1035 1040

Trp Arg Tyr Gln Leu Ile Arg Lys Asp Gly Glu Phe Arg Leu His Asn
1045 1050 1055

Pro Val Lys Glu Gln Glu Leu Ser Asp Lys Leu Gly Lys Ala Glu Ala
1060 1065 1070

Lys Lys Gln Ala Glu Lys Asp Asn Ala Gln Ser Leu Asp Ala Leu Ile
1075 1080 1085

Ala Ala Gly Arg Asp Ala Val Glu Lys Thr Glu Ser Val Ala Glu Pro
1090 1095 1100

Ala Arg Gln Ala Gly Gly Glu Asn Val Gly Ile Met Gln Ala Glu Glu
1105 1110 1115 1120

Glu Lys Lys Arg Val Gln Ala Asp Lys Asp Thr Ala Leu Ala Lys Gln

1125 1130 1135

Arg Glu Ala Glu Thr Arg Pro Ala Thr Thr Ala Phe Pro Arg Ala Arg
1140 1145 1150

Arg Ala Arg Arg Asp Leu Pro Gln Leu Gln Pro Gln Pro Gln Pro Gln
1155 1160 1165

Pro Gln Arg Asp Leu Ile Ser Arg Tyr Ala Asn Ser Gly Leu Ser Glu
1170 1175 1180

Phe Ser Ala Thr Leu Asn Ser Val Phe Ala Val Gln Asp Glu Leu Asp
1185 1190 1195 1200

Arg Val Phe Ala Glu Asp Arg Arg Asn Ala Val Trp Thr Ser Gly Ile
1205 1210 1215

Arg Asp Thr Lys His Tyr Arg Ser Gln Asp Phe Arg Ala Tyr Arg Gln
1220 1225 1230

Gln Thr Asp Leu Arg Gln Ile Gly Met Gln Lys Asn Leu Gly Ser Gly
1235 1240 1245

Arg Val Gly Ile Leu Phe Ser His Asn Arg Thr Glu Asn Thr Phe Asp
1250 1255 1260

Asp Gly Ile Gly Asn Ser Ala Arg Leu Ala His Gly Ala Val Phe Gly
1265 1270 1275 1280

Gln Tyr Gly Ile Asp Arg Phe Tyr Ile Gly Ile Ser Ala Gly Ala Gly
1285 1290 1295

Phe Ser Ser Gly Ser Leu Ser Asp Gly Ile Gly Gly Lys Ile Arg Arg
1300 1305 1310

Arg Val Leu His Tyr Gly Ile Gln Ala Arg Tyr Arg Ala Gly Phe Gly
1315 1320 1325

Gly Phe Gly Ile Glu Pro His Ile Gly Ala Thr Arg Tyr Phe Val Gln
1330 1335 1340

Lys Ala Asp Tyr Arg Tyr Glu Asn Val Asn Ile Ala Thr Pro Gly Leu
1345 1350 1355 1360

Ala Phe Asn Arg Tyr Arg Ala Gly Ile Lys Ala Asp Tyr Ser Phe Lys
1365 1370 1375

Pro Ala Gln His Ile Ser Ile Thr Pro Tyr Leu Ser Leu Ser Tyr Thr
1380 1385 1390

Asp Ala Ala Ser Gly Lys Val Arg Thr Arg Val Asn Thr Ala Val Leu
1395 1400 1405

Ala Gln Asp Phe Gly Lys Thr Arg Ser Ala Glu Trp Gly Val Asn Ala
1410 1415 1420

Glu Ile Lys Gly Phe Thr Leu Ser Leu His Ala Ala Ala Ala Lys Gly
1425 1430 1435 1440

Pro Gln Leu Glu Ala Gln His Ser Ala Gly Ile Lys Leu Gly Tyr Arg
1445 1450 1455

Trp

<210> 72
<211> 21
<212> PRT
<213> Escherichia coli

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Thr Val Ala Gln Ala
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<210>  73
<211>  1439
<212>  PRT
<213>  Neisseria meningitidis

<400>  73
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Thr Val Ala Gln Ala Ala Ser Ala Gly His Thr Tyr Phe Gly Ile Asn
            20                  25                  30

Tyr Gln Tyr Tyr Arg Asp Phe Ala Glu Asn Lys Gly Lys Phe Ala Val
        35                  40                  45

Gly Ala Lys Asp Ile Glu Val Tyr Asn Lys Lys Gly Glu Leu Val Gly
    50                  55                  60

Lys Ser Met Thr Lys Ala Pro Met Ile Asp Phe Ser Val Val Ser Arg
65                  70                  75                  80

Asn Gly Val Ala Ala Leu Val Gly Asp Gln Tyr Ile Val Ser Val Ala
                85                  90                  95

His Asn Gly Gly Tyr Asn Asn Val Asp Phe Gly Ala Glu Gly Arg Asn
            100                 105                 110

Pro Asp Gln His Arg Phe Thr Tyr Lys Ile Val Lys Arg Asn Asn Tyr
        115                 120                 125

Lys Ala Gly Thr Lys Gly His Pro Tyr Gly Gly Asp Tyr His Met Pro
    130                 135                 140

Arg Leu His Lys Phe Val Thr Asp Ala Glu Pro Val Glu Met Thr Ser
145                 150                 155                 160

Tyr Met Asp Gly Arg Lys Tyr Ile Asp Gln Asn Asn Tyr Pro Asp Arg
                165                 170                 175

Val Arg Ile Gly Ala Gly Arg Gln Tyr Trp Arg Ser Asp Glu Asp Glu
            180                 185                 190

Pro Asn Asn Arg Glu Ser Ser Tyr His Ile Ala Ser Ala Tyr Ser Trp
        195                 200                 205

Leu Val Gly Gly Asn Thr Phe Ala Gln Asn Gly Ser Gly Gly Gly Thr
    210                 215                 220

Val Asn Leu Gly Ser Glu Lys Ile Lys His Ser Pro Tyr Gly Phe Leu
225                 230                 235                 240

Pro Thr Gly Gly Ser Phe Gly Asp Ser Gly Ser Pro Met Phe Ile Tyr
                245                 250                 255

Asp Ala Gln Lys Gln Lys Trp Leu Ile Asn Gly Val Leu Gln Thr Gly
            260                 265                 270

Asn Pro Tyr Ile Gly Lys Ser Asn Gly Phe Gln Leu Val Arg Lys Asp
        275                 280                 285

Trp Phe Tyr Asp Glu Ile Phe Ala Gly Asp Thr His Ser Val Phe Tyr
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290 295 300

Glu Pro Arg Gln Asn Gly Lys Tyr Ser Phe Asn Asp Asp Asn Asn Gly
305 310 315 320

Thr Gly Lys Ile Asn Ala Lys His Glu His Asn Ser Leu Pro Asn Arg
325 330 335

Leu Lys Thr Arg Thr Val Gln Leu Phe Asn Val Ser Leu Ser Glu Thr
340 345 350

Ala Arg Glu Pro Val Tyr His Ala Ala Gly Gly Val Asn Ser Tyr Arg
355 360 365

Pro Arg Leu Asn Asn Gly Glu Asn Ile Ser Phe Ile Asp Glu Gly Lys
370 375 380

Gly Glu Leu Ile Leu Thr Ser Asn Ile Asn Gln Gly Ala Gly Gly Leu
385 390 395 400

Tyr Phe Gln Gly Asp Phe Thr Val Ser Pro Glu Asn Asn Glu Thr Trp
405 410 415

Gln Gly Ala Gly Val His Ile Ser Glu Asp Ser Thr Val Thr Trp Lys
420 425 430

Val Asn Gly Val Ala Asn Asp Arg Leu Ser Lys Ile Gly Lys Gly Thr
435 440 445

Leu His Val Gln Ala Lys Gly Glu Asn Gln Gly Ser Ile Ser Val Gly
450 455 460

Asp Gly Thr Val Ile Leu Asp Gln Gln Ala Asp Asp Lys Gly Lys Lys
465 470 475 480

Gln Ala Phe Ser Glu Ile Gly Leu Val Ser Gly Arg Gly Thr Val Gln
485 490 495

Leu Asn Ala Asp Asn Gln Phe Asn Pro Asp Lys Leu Tyr Phe Gly Phe
500 505 510

Arg Gly Gly Arg Leu Asp Leu Asn Gly His Ser Leu Ser Phe His Arg
515 520 525

Ile Gln Asn Thr Asp Glu Gly Ala Met Ile Val Asn His Asn Gln Asp
530 535 540

Lys Glu Ser Thr Val Thr Ile Thr Gly Asn Lys Asp Ile Ala Thr Thr
545 550 555 560

Gly Asn Asn Asn Ser Leu Asp Ser Lys Lys Glu Ile Ala Tyr Asn Gly
565 570 575

Trp Phe Gly Glu Lys Asp Thr Thr Lys Thr Asn Gly Arg Leu Asn Leu
580 585 590

Val Tyr Gln Pro Ala Ala Glu Asp Arg Thr Leu Leu Leu Ser Gly Gly
595 600 605

Thr Asn Leu Asn Gly Asn Ile Thr Gln Thr Asn Gly Lys Leu Phe Phe
610 615 620

Ser Gly Arg Pro Thr Pro His Ala Tyr Asn His Leu Asn Asp His Trp
625 630 635 640

Ser Gln Lys Glu Gly Ile Pro Arg Gly Glu Ile Val Trp Asp Asn Asp
645 650 655

Trp Ile Asn Arg Thr Phe Lys Ala Glu Asn Phe Gln Ile Lys Gly Gly

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                    660                 665                 670

Gln Ala Val Val Ser Arg Asn Val Ala Lys Val Lys Gly Asp Trp His
        675                 680                 685

Leu Ser Asn His Ala Gln Ala Val Phe Gly Val Ala Pro His Gln Ser
    690                 695                 700

His Thr Ile Cys Thr Arg Ser Asp Trp Thr Gly Leu Thr Asn Cys Val
705                 710                 715                 720

Glu Lys Thr Ile Thr Asp Asp Lys Val Ile Ala Ser Leu Thr Lys Thr
                725                 730                 735

Asp Ile Ser Gly Asn Val Asp Leu Ala Asp His Ala His Leu Asn Leu
            740                 745                 750

Thr Gly Leu Ala Thr Leu Asn Gly Asn Leu Ser Ala Asn Gly Asp Thr
        755                 760                 765

Arg Tyr Thr Val Ser His Asn Ala Thr Gln Asn Gly Asn Leu Ser Leu
    770                 775                 780

Val Gly Asn Ala Gln Ala Thr Phe Asn Gln Ala Thr Leu Asn Gly Asn
785                 790                 795                 800

Thr Ser Ala Ser Gly Asn Ala Ser Phe Asn Leu Ser Asp His Ala Val
                805                 810                 815

Gln Asn Gly Ser Leu Thr Leu Ser Gly Asn Ala Lys Ala Asn Val Ser
            820                 825                 830

His Ser Ala Leu Asn Gly Asn Val Ser Leu Ala Asp Lys Ala Val Phe
        835                 840                 845

His Phe Glu Ser Ser Arg Phe Thr Gly Gln Ile Ser Gly Gly Lys Asp
    850                 855                 860

Thr Ala Leu His Leu Lys Asp Ser Glu Trp Thr Leu Pro Ser Gly Thr
865                 870                 875                 880

Glu Leu Gly Asn Leu Asn Leu Asp Asn Ala Thr Ile Thr Leu Asn Ser
                885                 890                 895

Ala Tyr Arg His Asp Ala Ala Gly Ala Gln Thr Gly Ser Ala Thr Asp
            900                 905                 910

Ala Pro Arg Arg Arg Ser Arg Arg Ser Arg Arg Ser Leu Leu Ser Val
        915                 920                 925

Thr Pro Pro Thr Ser Val Glu Ser Arg Phe Asn Thr Leu Thr Val Asn
    930                 935                 940

Gly Lys Leu Asn Gly Gln Gly Thr Phe Arg Phe Met Ser Glu Leu Phe
945                 950                 955                 960

Gly Tyr Arg Ser Asp Lys Leu Lys Leu Ala Glu Ser Ser Glu Gly Thr
                965                 970                 975

Tyr Thr Leu Ala Val Asn Asn Thr Gly Asn Glu Pro Ala Ser Leu Glu
            980                 985                 990

Gln Leu Thr Val Val Glu Gly Lys Asp Asn Lys Pro Leu Ser Glu Asn
        995                 1000                1005

Leu Asn Phe Thr Leu Gln Asn Glu His Val Asp Ala Gly Ala Trp Arg
    1010                1015                1020

Tyr Gln Leu Ile Arg Lys Asp Gly Glu Phe Arg Leu His Asn Pro Val
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1025 1030 1035 1040

Lys Glu Gln Glu Leu Ser Asp Lys Leu Gly Lys Ala Glu Ala Lys Lys
1045 1050 1055

Gln Ala Glu Lys Asp Asn Ala Gln Ser Leu Asp Ala Leu Ile Ala Ala
1060 1065 1070

Gly Arg Asp Ala Val Glu Lys Thr Glu Ser Val Ala Glu Pro Ala Arg
1075 1080 1085

Gln Ala Gly Gly Glu Asn Val Gly Ile Met Gln Ala Glu Glu Glu Lys
1090 1095 1100

Lys Arg Val Gln Ala Asp Lys Asp Thr Ala Leu Ala Lys Gln Arg Glu
1105 1110 1115 1120

Ala Glu Thr Arg Pro Ala Thr Thr Ala Phe Pro Arg Ala Arg Arg Ala
1125 1130 1135

Arg Arg Asp Leu Pro Gln Leu Gln Pro Gln Pro Gln Pro Gln Pro Gln
1140 1145 1150

Arg Asp Leu Ile Ser Arg Tyr Ala Asn Ser Gly Leu Ser Glu Phe Ser
1155 1160 1165

Ala Thr Leu Asn Ser Val Phe Ala Val Gln Asp Glu Leu Asp Arg Val
1170 1175 1180

Phe Ala Glu Asp Arg Arg Asn Ala Val Trp Thr Ser Gly Ile Arg Asp
1185 1190 1195 1200

Thr Lys His Tyr Arg Ser Gln Asp Phe Arg Ala Tyr Arg Gln Gln Thr
1205 1210 1215

Asp Leu Arg Gln Ile Gly Met Gln Lys Asn Leu Gly Ser Gly Arg Val
1220 1225 1230

Gly Ile Leu Phe Ser His Asn Arg Thr Glu Asn Thr Phe Asp Asp Gly
1235 1240 1245

Ile Gly Asn Ser Ala Arg Leu Ala His Gly Ala Val Phe Gly Gln Tyr
1250 1255 1260

Gly Ile Asp Arg Phe Tyr Ile Gly Ile Ser Ala Gly Ala Gly Phe Ser
1265 1270 1275 1280

Ser Gly Ser Leu Ser Asp Gly Ile Gly Gly Lys Ile Arg Arg Arg Val
1285 1290 1295

Leu His Tyr Gly Ile Gln Ala Arg Tyr Arg Ala Gly Phe Gly Gly Phe
1300 1305 1310

Gly Ile Glu Pro His Ile Gly Ala Thr Arg Tyr Phe Val Gln Lys Ala
1315 1320 1325

Asp Tyr Arg Tyr Glu Asn Val Asn Ile Ala Thr Pro Gly Leu Ala Phe
1330 1335 1340

Asn Arg Tyr Arg Ala Gly Ile Lys Ala Asp Tyr Ser Phe Lys Pro Ala
1345 1350 1355 1360

Gln His Ile Ser Ile Thr Pro Tyr Leu Ser Leu Ser Tyr Thr Asp Ala
1365 1370 1375

Ala Ser Gly Lys Val Arg Thr Arg Val Asn Thr Ala Val Leu Ala Gln
1380 1385 1390

Asp Phe Gly Lys Thr Arg Ser Ala Glu Trp Gly Val Asn Ala Glu Ile

1395 1400 1405

Lys Gly Phe Thr Leu Ser Leu His Ala Ala Ala Ala Lys Gly Pro Gln
1410 1415 1420

Leu Glu Ala Gln His Ser Ala Gly Ile Lys Leu Gly Tyr Arg Trp
1425 1430 1435

<210> 74
<211> 164
<212> PRT
<213> Neisseria meningitidis

<400> 74
Met Lys Lys Asn Ile Leu Glu Phe Trp Val Gly Leu Phe Val Leu Ile
1 5 10 15

Gly Ala Ala Ala Val Ala Phe Leu Ala Phe Arg Val Ala Gly Gly Ala
20 25 30

Ala Phe Gly Gly Ser Asp Lys Thr Tyr Ala Val Tyr Ala Asp Phe Gly
35 40 45

Asp Ile Gly Gly Leu Lys Val Asn Ala Pro Val Lys Ser Ala Gly Val
50 55 60

Leu Val Gly Arg Val Gly Ala Ile Gly Leu Asp Pro Lys Ser Tyr Gln
65 70 75 80

Ala Arg Val Arg Leu Asp Leu Asp Gly Lys Tyr Gln Phe Ser Ser Asp
85 90 95

Val Ser Ala Gln Ile Leu Thr Ser Gly Leu Leu Gly Glu Gln Tyr Ile
100 105 110

Gly Leu Gln Gln Gly Gly Asp Thr Glu Asn Leu Ala Ala Gly Asp Thr
115 120 125

Ile Ser Val Thr Ser Ser Ala Met Val Leu Glu Asn Leu Ile Gly Lys
130 135 140

Phe Met Thr Ser Phe Ala Glu Lys Asn Ala Asp Gly Gly Asn Ala Glu
145 150 155 160

Lys Ala Ala Glu

<210> 75
<211> 21
<212> PRT
<213> Erwinia carotovora

<400> 75
Met Lys Tyr Leu Leu Pro Thr Ala Ala Ala Gly Leu Leu Leu Ala Ala
1 5 10 15

Gln Pro Ala Met Ala
20

<210> 76
<211> 608
<212> PRT
<213> Neisseria meningitidis ORF46

<400> 76
Leu Gly Ile Ser Arg Lys Ile Ser Leu Ile Leu Ser Ile Leu Ala Val
1 5 10 15

Cys Leu Pro Met His Ala His Ala Ser Asp Leu Ala Asn Asp Ser Phe

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            20                  25                  30

Ile Arg Gln Val Leu Asp Arg Gln His Phe Glu Pro Asp Gly Lys Tyr
        35                  40                  45

His Leu Phe Gly Ser Arg Gly Glu Leu Ala Glu Arg Ser Gly His Ile
    50                  55                  60

Gly Leu Gly Lys Ile Gln Ser His Gln Leu Gly Asn Leu Met Ile Gln
65                  70                  75                  80

Gln Ala Ala Ile Lys Gly Asn Ile Gly Tyr Ile Val Arg Phe Ser Asp
                85                  90                  95

His Gly His Glu Val His Ser Pro Phe Asp Asn His Ala Ser His Ser
            100                 105                 110

Asp Ser Asp Glu Ala Gly Ser Pro Val Asp Gly Phe Ser Leu Tyr Arg
        115                 120                 125

Ile His Trp Asp Gly Tyr Glu His His Pro Ala Asp Gly Tyr Asp Gly
    130                 135                 140

Pro Gln Gly Gly Gly Tyr Pro Ala Pro Lys Gly Ala Arg Asp Ile Tyr
145                 150                 155                 160

Ser Tyr Asp Ile Lys Gly Val Ala Gln Asn Ile Arg Leu Asn Leu Thr
                165                 170                 175

Asp Asn Arg Ser Thr Gly Gln Arg Leu Ala Asp Arg Phe His Asn Ala
            180                 185                 190

Gly Ser Met Leu Thr Gln Gly Val Gly Asp Gly Phe Lys Arg Ala Thr
        195                 200                 205

Arg Tyr Ser Pro Glu Leu Asp Arg Ser Gly Asn Ala Ala Glu Ala Phe
    210                 215                 220

Asn Gly Thr Ala Asp Ile Val Lys Asn Ile Ile Gly Ala Ala Gly Glu
225                 230                 235                 240

Ile Val Gly Ala Gly Asp Ala Val Gln Gly Ile Ser Glu Gly Ser Asn
                245                 250                 255

Ile Ala Val Met His Gly Leu Gly Leu Leu Ser Thr Glu Asn Lys Met
            260                 265                 270

Ala Arg Ile Asn Asp Leu Ala Asp Met Ala Gln Leu Lys Asp Tyr Ala
        275                 280                 285

Ala Ala Ala Ile Arg Asp Trp Ala Val Gln Asn Pro Asn Ala Ala Gln
    290                 295                 300

Gly Ile Glu Ala Val Ser Asn Ile Phe Met Ala Ala Ile Pro Ile Lys
305                 310                 315                 320

Gly Ile Gly Ala Val Arg Gly Lys Tyr Gly Leu Gly Gly Ile Thr Ala
                325                 330                 335

His Pro Ile Lys Arg Ser Gln Met Gly Ala Ile Ala Leu Pro Lys Gly
            340                 345                 350

Lys Ser Ala Val Ser Asp Asn Phe Ala Asp Ala Ala Tyr Ala Lys Tyr
        355                 360                 365

Pro Ser Pro Tyr His Ser Arg Asn Ile Arg Ser Asn Leu Glu Gln Arg
    370                 375                 380

Tyr Gly Lys Glu Asn Ile Thr Ser Ser Thr Val Pro Pro Ser Asn Gly
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385                 390                 395                 400

Lys Asn Val Lys Leu Ala Asp Gln Arg His Pro Lys Thr Gly Val Pro
                405                 410                 415

Phe Asp Gly Lys Gly Phe Pro Asn Phe Glu Lys His Val Lys Tyr Asp
            420                 425                 430

Thr Lys Leu Asp Ile Gln Glu Leu Ser Gly Gly Gly Ile Pro Lys Ala
        435                 440                 445

Lys Pro Val Ser Asp Ala Lys Pro Arg Trp Glu Val Asp Arg Lys Leu
    450                 455                 460

Asn Lys Leu Thr Thr Arg Glu Gln Val Glu Lys Asn Val Gln Glu Ile
465                 470                 475                 480

Arg Asn Gly Asn Lys Asn Ser Asn Phe Ser Gln His Ala Gln Leu Glu
                485                 490                 495

Arg Glu Ile Asn Lys Leu Lys Ser Ala Asp Glu Ile Asn Phe Ala Asp
            500                 505                 510

Gly Met Gly Lys Phe Thr Asp Ser Met Asn Asp Lys Ala Phe Ser Arg
        515                 520                 525

Leu Val Lys Ser Val Lys Glu Asn Gly Phe Thr Asn Pro Val Val Glu
    530                 535                 540

Tyr Val Glu Ile Asn Gly Lys Ala Tyr Ile Val Arg Gly Asn Asn Arg
545                 550                 555                 560

Val Phe Ala Ala Glu Tyr Leu Gly Arg Ile His Glu Leu Lys Phe Lys
                565                 570                 575

Lys Val Asp Phe Pro Val Pro Asn Thr Ser Trp Lys Asn Pro Thr Asp
            580                 585                 590

Val Leu Asn Glu Ser Gly Asn Val Lys Arg Pro Arg Tyr Arg Ser Lys
        595                 600                 605


<210>   77
<211>   584
<212>   PRT
<213>   Artificial Sequence

<220>
<223>   ORF46-2

<400>   77
Ser Asp Leu Ala Asn Asp Ser Phe Ile Arg Gln Val Leu Asp Arg Gln
1               5                   10                  15

His Phe Glu Pro Asp Gly Lys Tyr His Leu Phe Gly Ser Arg Gly Glu
            20                  25                  30

Leu Ala Glu Arg Ser Gly His Ile Gly Leu Gly Lys Ile Gln Ser His
        35                  40                  45

Gln Leu Gly Asn Leu Met Ile Gln Gln Ala Ala Ile Lys Gly Asn Ile
    50                  55                  60

Gly Tyr Ile Val Arg Phe Ser Asp His Gly His Glu Val His Ser Pro
65                  70                  75                  80

Phe Asp Asn His Ala Ser His Ser Asp Ser Asp Glu Ala Gly Ser Pro
                85                  90                  95
```

Val Asp Gly Phe Ser Leu Tyr Arg Ile His Trp Asp Gly Tyr Glu His
100 105 110

His Pro Ala Asp Gly Tyr Asp Gly Pro Gln Gly Gly Gly Tyr Pro Ala
115 120 125

Pro Lys Gly Ala Arg Asp Ile Tyr Ser Tyr Asp Ile Lys Gly Val Ala
130 135 140

Gln Asn Ile Arg Leu Asn Leu Thr Asp Asn Arg Ser Thr Gly Gln Arg
145 150 155 160

Leu Ala Asp Arg Phe His Asn Ala Gly Ser Met Leu Thr Gln Gly Val
165 170 175

Gly Asp Gly Phe Lys Arg Ala Thr Arg Tyr Ser Pro Glu Leu Asp Arg
180 185 190

Ser Gly Asn Ala Ala Glu Ala Phe Asn Gly Thr Ala Asp Ile Val Lys
195 200 205

Asn Ile Ile Gly Ala Ala Gly Glu Ile Val Gly Ala Gly Asp Ala Val
210 215 220

Gln Gly Ile Ser Glu Gly Ser Asn Ile Ala Val Met His Gly Leu Gly
225 230 235 240

Leu Leu Ser Thr Glu Asn Lys Met Ala Arg Ile Asn Asp Leu Ala Asp
245 250 255

Met Ala Gln Leu Lys Asp Tyr Ala Ala Ala Ala Ile Arg Asp Trp Ala
260 265 270

Val Gln Asn Pro Asn Ala Ala Gln Gly Ile Glu Ala Val Ser Asn Ile
275 280 285

Phe Met Ala Ala Ile Pro Ile Lys Gly Ile Gly Ala Val Arg Gly Lys
290 295 300

Tyr Gly Leu Gly Gly Ile Thr Ala His Pro Ile Lys Arg Ser Gln Met
305 310 315 320

Gly Ala Ile Ala Leu Pro Lys Gly Lys Ser Ala Val Ser Asp Asn Phe
325 330 335

Ala Asp Ala Ala Tyr Ala Lys Tyr Pro Ser Pro Tyr His Ser Arg Asn
340 345 350

Ile Arg Ser Asn Leu Glu Gln Arg Tyr Gly Lys Glu Asn Ile Thr Ser
355 360 365

Ser Thr Val Pro Pro Ser Asn Gly Lys Asn Val Lys Leu Ala Asp Gln
370 375 380

Arg His Pro Lys Thr Gly Val Pro Phe Asp Gly Lys Gly Phe Pro Asn
385 390 395 400

Phe Glu Lys His Val Lys Tyr Asp Thr Lys Leu Asp Ile Gln Glu Leu
405 410 415

Ser Gly Gly Gly Ile Pro Lys Ala Lys Pro Val Ser Asp Ala Lys Pro
420 425 430

Arg Trp Glu Val Asp Arg Lys Leu Asn Lys Leu Thr Thr Arg Glu Gln
435 440 445

Val Glu Lys Asn Val Gln Glu Ile Arg Asn Gly Asn Lys Asn Ser Asn
450 455 460

Phe Ser Gln His Ala Gln Leu Glu Arg Glu Ile Asn Lys Leu Lys Ser
465   470   475   480

Ala Asp Glu Ile Asn Phe Ala Asp Gly Met Gly Lys Phe Thr Asp Ser
                485   490   495

Met Asn Asp Lys Ala Phe Ser Arg Leu Val Lys Ser Val Lys Glu Asn
            500   505   510

Gly Phe Thr Asn Pro Val Val Glu Tyr Val Glu Ile Asn Gly Lys Ala
        515   520   525

Tyr Ile Val Arg Gly Asn Asn Arg Val Phe Ala Ala Glu Tyr Leu Gly
    530   535   540

Arg Ile His Glu Leu Lys Phe Lys Lys Val Asp Phe Pro Val Pro Asn
545   550   555   560

Thr Ser Trp Lys Asn Pro Thr Asp Val Leu Asn Glu Ser Gly Asn Val
                565   570   575

Lys Arg Pro Arg Tyr Arg Ser Lys
            580

<210> 78
<211> 364
<212> PRT
<213> Neisseria meningitidis

<400> 78
Met Ser Met Lys His Phe Pro Ala Lys Val Leu Thr Thr Ala Ile Leu
1   5   10   15

Ala Thr Phe Cys Ser Gly Ala Leu Ala Ala Thr Ser Asp Asp Asp Val
            20   25   30

Lys Lys Ala Ala Thr Val Ala Ile Val Ala Ala Tyr Asn Asn Gly Gln
        35   40   45

Glu Ile Asn Gly Phe Lys Ala Gly Glu Thr Ile Tyr Asp Ile Gly Glu
    50   55   60

Asp Gly Thr Ile Thr Gln Lys Asp Ala Thr Ala Ala Asp Val Glu Ala
65   70   75   80

Asp Asp Phe Lys Gly Leu Gly Leu Lys Lys Val Val Thr Asn Leu Thr
                85   90   95

Lys Thr Val Asn Glu Asn Lys Gln Asn Val Asp Ala Lys Val Lys Ala
            100   105   110

Ala Glu Ser Glu Ile Glu Lys Leu Thr Thr Lys Leu Ala Asp Thr Asp
        115   120   125

Ala Ala Leu Ala Asp Thr Asp Ala Ala Leu Asp Glu Thr Thr Asn Ala
    130   135   140

Leu Asn Lys Leu Gly Glu Asn Ile Thr Thr Phe Ala Glu Glu Thr Lys
145   150   155   160

Thr Asn Ile Val Lys Ile Asp Glu Lys Leu Glu Ala Val Ala Asp Thr
                165   170   175

Val Asp Lys His Ala Glu Ala Phe Asn Asp Ile Ala Asp Ser Leu Asp
            180   185   190

Glu Thr Asn Thr Lys Ala Asp Glu Ala Val Lys Thr Ala Asn Glu Ala
        195   200   205

Lys Gln Thr Ala Glu Glu Thr Lys Gln Asn Val Asp Ala Lys Val Lys
210 215 220

Ala Ala Glu Thr Ala Ala Gly Lys Ala Glu Ala Ala Ala Gly Thr Ala
225 230 235 240

Asn Thr Ala Ala Asp Lys Ala Glu Ala Val Ala Ala Lys Val Thr Asp
245 250 255

Ile Lys Ala Asp Ile Ala Thr Asn Lys Ala Asp Ile Ala Lys Asn Ser
260 265 270

Ala Arg Ile Asp Ser Leu Asp Lys Asn Val Ala Asn Leu Arg Lys Glu
275 280 285

Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly Leu Phe Gln
290 295 300

Pro Tyr Asn Val Gly Arg Phe Asn Val Thr Ala Ala Val Gly Gly Tyr
305 310 315 320

Lys Ser Glu Ser Ala Val Ala Ile Gly Thr Gly Phe Arg Phe Thr Glu
325 330 335

Asn Phe Ala Ala Lys Ala Gly Val Ala Val Gly Thr Ser Ser Gly Ser
340 345 350

Ser Ala Ala Tyr His Val Gly Val Asn Tyr Glu Trp
355 360

<210> 79
<211> 427
<212> PRT
<213> Neisseria meningitidis

<400> 79
Met Phe Glu Arg Ser Val Ile Ala Met Ala Cys Ile Phe Ala Leu Ser
1 5 10 15

Ala Cys Gly Gly Gly Gly Gly Gly Ser Pro Asp Val Lys Ser Ala Asp
20 25 30

Thr Leu Ser Lys Pro Ala Ala Pro Val Val Ala Glu Lys Glu Thr Glu
35 40 45

Val Lys Glu Asp Ala Pro Gln Ala Gly Ser Gln Gly Gln Gly Ala Pro
50 55 60

Ser Thr Gln Gly Ser Gln Asp Met Ala Ala Val Ser Ala Glu Asn Thr
65 70 75 80

Gly Asn Gly Gly Ala Ala Thr Thr Asp Lys Pro Lys Asn Glu Asp Glu
85 90 95

Gly Pro Gln Asn Asp Met Pro Gln Asn Ser Ala Glu Ser Ala Asn Gln
100 105 110

Thr Gly Asn Asn Gln Pro Ala Asp Ser Ser Asp Ser Ala Pro Ala Ser
115 120 125

Asn Pro Ala Pro Ala Asn Gly Gly Ser Asn Phe Gly Arg Val Asp Leu
130 135 140

Ala Asn Gly Val Leu Ile Asp Gly Pro Ser Gln Asn Ile Thr Leu Thr
145 150 155 160

His Cys Lys Gly Asp Ser Cys Asn Gly Asp Asn Leu Leu Asp Glu Glu
165 170 175

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Ala Pro Ser Lys Ser Glu Phe Glu Asn Leu Asn Glu Ser Glu Arg Ile
            180                 185                 190

Glu Lys Tyr Lys Lys Asp Gly Lys Ser Asp Lys Phe Thr Asn Leu Val
        195                 200                 205

Ala Thr Ala Val Gln Ala Asn Gly Thr Asn Lys Tyr Val Ile Ile Tyr
    210                 215                 220

Lys Asp Lys Ser Ala Ser Ser Ser Ser Ala Arg Phe Arg Arg Ser Ala
225                 230                 235                 240

Arg Ser Arg Arg Ser Leu Pro Ala Glu Met Pro Leu Ile Pro Val Asn
                245                 250                 255

Gln Ala Asp Thr Leu Ile Val Asp Gly Glu Ala Val Ser Leu Thr Gly
            260                 265                 270

His Ser Gly Asn Ile Phe Ala Pro Glu Gly Asn Tyr Arg Tyr Leu Thr
        275                 280                 285

Tyr Gly Ala Glu Lys Leu Pro Gly Gly Ser Tyr Ala Leu Arg Val Gln
    290                 295                 300

Gly Glu Pro Ala Lys Gly Glu Met Leu Ala Gly Thr Ala Val Tyr Asn
305                 310                 315                 320

Gly Glu Val Leu His Phe His Thr Glu Asn Gly Arg Pro Tyr Pro Thr
                325                 330                 335

Arg Gly Arg Phe Ala Ala Lys Val Asp Phe Gly Ser Lys Ser Val Asp
            340                 345                 350

Gly Ile Ile Asp Ser Gly Asp Asp Leu His Met Gly Thr Gln Lys Phe
        355                 360                 365

Lys Ala Ala Ile Asp Gly Asn Gly Phe Lys Gly Thr Trp Thr Glu Asn
    370                 375                 380

Gly Gly Gly Asp Val Ser Gly Arg Phe Tyr Gly Pro Ala Gly Glu Glu
385                 390                 395                 400

Val Ala Gly Lys Tyr Ser Tyr Arg Pro Thr Asp Ala Glu Lys Gly Gly
                405                 410                 415

Phe Gly Val Phe Ala Gly Lys Lys Glu Gln Asp
            420                 425

<210>  80
<211>  410
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  287untagged

<400>  80
Cys Gly Gly Gly Gly Gly Gly Ser Pro Asp Val Lys Ser Ala Asp Thr
1               5                   10                  15

Leu Ser Lys Pro Ala Ala Pro Val Val Ala Glu Lys Glu Thr Glu Val
            20                  25                  30

Lys Glu Asp Ala Pro Gln Ala Gly Ser Gln Gly Gln Gly Ala Pro Ser
        35                  40                  45

Thr Gln Gly Ser Gln Asp Met Ala Ala Val Ser Ala Glu Asn Thr Gly
    50                  55                  60
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Asn Gly Gly Ala Ala Thr Thr Asp Lys Pro Lys Asn Glu Asp Glu Gly
65                  70                  75                  80

Pro Gln Asn Asp Met Pro Gln Asn Ser Ala Glu Ser Ala Asn Gln Thr
                85                  90                  95

Gly Asn Asn Gln Pro Ala Asp Ser Ser Asp Ser Ala Pro Ala Ser Asn
            100                 105                 110

Pro Ala Pro Ala Asn Gly Gly Ser Asn Phe Gly Arg Val Asp Leu Ala
        115                 120                 125

Asn Gly Val Leu Ile Asp Gly Pro Ser Gln Asn Ile Thr Leu Thr His
    130                 135                 140

Cys Lys Gly Asp Ser Cys Asn Gly Asp Asn Leu Leu Asp Glu Glu Ala
145                 150                 155                 160

Pro Ser Lys Ser Glu Phe Glu Asn Leu Asn Glu Ser Glu Arg Ile Glu
                165                 170                 175

Lys Tyr Lys Lys Asp Gly Lys Ser Asp Lys Phe Thr Asn Leu Val Ala
            180                 185                 190

Thr Ala Val Gln Ala Asn Gly Thr Asn Lys Tyr Val Ile Ile Tyr Lys
        195                 200                 205

Asp Lys Ser Ala Ser Ser Ser Ser Ala Arg Phe Arg Arg Ser Ala Arg
    210                 215                 220

Ser Arg Arg Ser Leu Pro Ala Glu Met Pro Leu Ile Pro Val Asn Gln
225                 230                 235                 240

Ala Asp Thr Leu Ile Val Asp Gly Glu Ala Val Ser Leu Thr Gly His
                245                 250                 255

Ser Gly Asn Ile Phe Ala Pro Glu Gly Asn Tyr Arg Tyr Leu Thr Tyr
            260                 265                 270

Gly Ala Glu Lys Leu Pro Gly Gly Ser Tyr Ala Leu Arg Val Gln Gly
        275                 280                 285

Glu Pro Ala Lys Gly Glu Met Leu Ala Gly Thr Ala Val Tyr Asn Gly
    290                 295                 300

Glu Val Leu His Phe His Thr Glu Asn Gly Arg Pro Tyr Pro Thr Arg
305                 310                 315                 320

Gly Arg Phe Ala Ala Lys Val Asp Phe Gly Ser Lys Ser Val Asp Gly
                325                 330                 335

Ile Ile Asp Ser Gly Asp Asp Leu His Met Gly Thr Gln Lys Phe Lys
            340                 345                 350

Ala Ala Ile Asp Gly Asn Gly Phe Lys Gly Thr Trp Thr Glu Asn Gly
        355                 360                 365

Gly Gly Asp Val Ser Gly Arg Phe Tyr Gly Pro Ala Gly Glu Glu Val
    370                 375                 380

Ala Gly Lys Tyr Ser Tyr Arg Pro Thr Asp Ala Glu Lys Gly Gly Phe
385                 390                 395                 400

Gly Val Phe Ala Gly Lys Lys Glu Gln Asp
                405                 410
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<210> 81
<211> 9
<212> PRT

<213> Artificial Sequence

<220>
<223> 920L N-terminal

<400> 81
His Arg Val Trp Val Glu Thr Ala His
1 5

<210> 82
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> 953L N-terminal

<400> 82
Ala Thr Tyr Lys Val Asp Glu Tyr His Ala Asn Ala Arg Phe Ala Phe
1 5 10 15

<210> 83
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> 519.1L N-terminal

<400> 83
Met Glu Phe Phe Ile Ile Leu Leu Ala
1 5

<210> 84
<211> 488
<212> PRT
<213> Artificial Sequence

<220>
<223> deltaG287

<400> 84
Met Phe Lys Arg Ser Val Ile Ala Met Ala Cys Ile Phe Ala Leu Ser
1 5 10 15

Ala Cys Gly Gly Gly Gly Gly Gly Ser Pro Asp Val Lys Ser Ala Asp
20 25 30

Thr Leu Ser Lys Pro Ala Ala Pro Val Val Ser Glu Lys Glu Thr Glu
35 40 45

Ala Lys Glu Asp Ala Pro Gln Ala Gly Ser Gln Gly Gln Gly Ala Pro
50 55 60

Ser Ala Gln Gly Ser Gln Asp Met Ala Ala Val Ser Glu Glu Asn Thr
65 70 75 80

Gly Asn Gly Gly Ala Val Thr Ala Asp Asn Pro Lys Asn Glu Asp Glu
85 90 95

Val Ala Gln Asn Asp Met Pro Gln Asn Ala Ala Gly Thr Asp Ser Ser
100 105 110

Thr Pro Asn His Thr Pro Asp Pro Asn Met Leu Ala Gly Asn Met Glu
115 120 125

Asn Gln Ala Thr Asp Ala Gly Glu Ser Ser Gln Pro Ala Asn Gln Pro
130 135 140

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Asp Met Ala Asn Ala Ala Asp Gly Met Gln Gly Asp Asp Pro Ser Ala
145                 150                 155                 160

Gly Gly Gln Asn Ala Gly Asn Thr Ala Ala Gln Gly Ala Asn Gln Ala
                165                 170                 175

Gly Asn Asn Gln Ala Ala Gly Ser Ser Asp Pro Ile Pro Ala Ser Asn
            180                 185                 190

Pro Ala Pro Ala Asn Gly Gly Ser Asn Phe Gly Arg Val Asp Leu Ala
        195                 200                 205

Asn Gly Val Leu Ile Asp Gly Pro Ser Gln Asn Ile Thr Leu Thr His
    210                 215                 220

Cys Lys Gly Asp Ser Cys Ser Gly Asn Asn Phe Leu Asp Glu Glu Val
225                 230                 235                 240

Gln Leu Lys Ser Glu Phe Glu Lys Leu Ser Asp Ala Asp Lys Ile Ser
                245                 250                 255

Asn Tyr Lys Lys Asp Gly Lys Asn Asp Lys Phe Val Gly Leu Val Ala
            260                 265                 270

Asp Ser Val Gln Met Lys Gly Ile Asn Gln Tyr Ile Ile Phe Tyr Lys
        275                 280                 285

Pro Lys Pro Thr Ser Phe Ala Arg Phe Arg Arg Ser Ala Arg Ser Arg
    290                 295                 300

Arg Ser Leu Pro Ala Glu Met Pro Leu Ile Pro Val Asn Gln Ala Asp
305                 310                 315                 320

Thr Leu Ile Val Asp Gly Glu Ala Val Ser Leu Thr Gly His Ser Gly
                325                 330                 335

Asn Ile Phe Ala Pro Glu Gly Asn Tyr Arg Tyr Leu Thr Tyr Gly Ala
            340                 345                 350

Glu Lys Leu Pro Gly Gly Ser Tyr Ala Leu Arg Val Gln Gly Glu Pro
        355                 360                 365

Ala Lys Gly Glu Met Leu Ala Gly Ala Ala Val Tyr Asn Gly Glu Val
    370                 375                 380

Leu His Phe His Thr Glu Asn Gly Arg Pro Tyr Pro Thr Arg Gly Arg
385                 390                 395                 400

Phe Ala Ala Lys Val Asp Phe Gly Ser Lys Ser Val Asp Gly Ile Ile
                405                 410                 415

Asp Ser Gly Asp Asp Leu His Met Gly Thr Gln Lys Phe Lys Ala Ala
            420                 425                 430

Ile Asp Gly Asn Gly Phe Lys Gly Thr Trp Thr Glu Asn Gly Ser Gly
        435                 440                 445

Asp Val Ser Gly Lys Phe Tyr Gly Pro Ala Gly Glu Glu Val Ala Gly
    450                 455                 460

Lys Tyr Ser Tyr Arg Pro Thr Asp Ala Glu Lys Gly Gly Phe Gly Val
465                 470                 475                 480

Phe Ala Gly Lys Lys Glu Gln Asp
                485

<210>   85
<211>   712
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<212> PRT
<213> Artificial Sequence

<220>
<223> TBP2

<400> 85

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Met Asn Asn Pro Leu Val Asn Gln Ala Ala Met Val Leu Pro Val Phe
1               5                   10                  15

Leu Leu Ser Ala Cys Leu Gly Gly Gly Gly Ser Phe Asp Leu Asp Ser
            20                  25                  30

Val Asp Thr Glu Ala Pro Arg Pro Ala Pro Lys Tyr Gln Asp Val Phe
        35                  40                  45

Ser Glu Lys Pro Gln Ala Gln Lys Asp Gln Gly Gly Tyr Gly Phe Ala
    50                  55                  60

Met Arg Leu Lys Arg Arg Asn Trp Tyr Pro Gln Ala Lys Glu Asp Glu
65                  70                  75                  80

Val Lys Leu Asp Glu Ser Asp Trp Glu Ala Thr Gly Leu Pro Asp Glu
                85                  90                  95

Pro Lys Glu Leu Pro Lys Arg Gln Lys Ser Val Ile Glu Lys Val Glu
            100                 105                 110

Thr Asp Ser Asp Asn Asn Ile Tyr Ser Ser Pro Tyr Leu Lys Pro Ser
        115                 120                 125

Asn His Gln Asn Gly Asn Thr Gly Asn Gly Ile Asn Gln Pro Lys Asn
    130                 135                 140

Gln Ala Lys Asp Tyr Glu Asn Phe Lys Tyr Val Tyr Ser Gly Trp Phe
145                 150                 155                 160

Tyr Lys His Ala Lys Arg Glu Phe Asn Leu Lys Val Glu Pro Lys Ser
                165                 170                 175

Ala Lys Asn Gly Asp Asp Gly Tyr Ile Phe Tyr His Gly Lys Glu Pro
            180                 185                 190

Ser Arg Gln Leu Pro Ala Ser Gly Lys Ile Thr Tyr Lys Gly Val Trp
        195                 200                 205

His Phe Ala Thr Asp Thr Lys Lys Gly Gln Lys Phe Arg Glu Ile Ile
    210                 215                 220

Gln Pro Ser Lys Ser Gln Gly Asp Arg Tyr Ser Gly Phe Ser Gly Asp
225                 230                 235                 240

Asp Gly Glu Glu Tyr Ser Asn Lys Asn Lys Ser Thr Leu Thr Asp Gly
                245                 250                 255

Gln Glu Gly Tyr Gly Phe Thr Ser Asn Leu Glu Val Asp Phe His Asn
            260                 265                 270

Lys Lys Leu Thr Gly Lys Leu Ile Arg Asn Asn Ala Asn Thr Asp Asn
        275                 280                 285

Asn Gln Ala Thr Thr Thr Gln Tyr Tyr Ser Leu Glu Ala Gln Val Thr
    290                 295                 300

Gly Asn Arg Phe Asn Gly Lys Ala Thr Ala Thr Asp Lys Pro Gln Gln
305                 310                 315                 320

Asn Ser Glu Thr Lys Glu His Pro Phe Val Ser Asp Ser Ser Ser Leu
                325                 330                 335
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Ser Gly Gly Phe Phe Gly Pro Gln Gly Glu Glu Leu Gly Phe Arg Phe
            340                 345                 350

Leu Ser Asp Asp Gln Lys Val Ala Val Val Gly Ser Ala Lys Thr Lys
        355                 360                 365

Asp Lys Pro Ala Asn Gly Asn Thr Ala Ala Ala Ser Gly Gly Thr Asp
    370                 375                 380

Ala Ala Ala Ser Asn Gly Ala Ala Gly Thr Ser Ser Glu Asn Gly Lys
385                 390                 395                 400

Leu Thr Thr Val Leu Asp Ala Val Glu Leu Lys Leu Gly Asp Lys Glu
                405                 410                 415

Val Gln Lys Leu Asp Asn Phe Ser Asn Ala Ala Gln Leu Val Val Asp
            420                 425                 430

Gly Ile Met Ile Pro Leu Leu Pro Glu Ala Ser Glu Ser Gly Asn Asn
        435                 440                 445

Gln Ala Asn Gln Gly Thr Asn Gly Gly Thr Ala Phe Thr Arg Lys Phe
    450                 455                 460

Asp His Thr Pro Glu Ser Asp Lys Lys Asp Ala Gln Ala Gly Thr Gln
465                 470                 475                 480

Thr Asn Gly Ala Gln Thr Ala Ser Asn Thr Ala Gly Asp Thr Asn Gly
                485                 490                 495

Lys Thr Lys Thr Tyr Glu Val Glu Val Cys Cys Ser Asn Leu Asn Tyr
            500                 505                 510

Leu Lys Tyr Gly Met Leu Thr Arg Lys Asn Ser Lys Ser Ala Met Gln
        515                 520                 525

Ala Gly Glu Ser Ser Ser Gln Ala Asp Ala Lys Thr Glu Gln Val Glu
    530                 535                 540

Gln Ser Met Phe Leu Gln Gly Glu Arg Thr Asp Glu Lys Glu Ile Pro
545                 550                 555                 560

Ser Glu Gln Asn Ile Val Tyr Arg Gly Ser Trp Tyr Gly Tyr Ile Ala
                565                 570                 575

Asn Asp Lys Ser Thr Ser Trp Ser Gly Asn Ala Ser Asn Ala Thr Ser
            580                 585                 590

Gly Asn Arg Ala Glu Phe Thr Val Asn Phe Ala Asp Lys Lys Ile Thr
        595                 600                 605

Gly Thr Leu Thr Ala Asp Asn Arg Gln Glu Ala Thr Phe Thr Ile Asp
    610                 615                 620

Gly Asn Ile Lys Asp Asn Gly Phe Glu Gly Thr Ala Lys Thr Ala Glu
625                 630                 635                 640

Ser Gly Phe Asp Leu Asp Gln Ser Asn Thr Thr Arg Thr Pro Lys Ala
                645                 650                 655

Tyr Ile Thr Asp Ala Lys Val Gln Gly Gly Phe Tyr Gly Pro Lys Ala
            660                 665                 670

Glu Glu Leu Gly Gly Trp Phe Ala Tyr Pro Gly Asp Lys Gln Thr Lys
        675                 680                 685

Asn Ala Thr Asn Ala Ser Gly Asn Ser Ser Ala Thr Val Val Phe Gly
    690                 695                 700
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Ala Lys Arg Gln Gln Pro Val Arg
705 710

<210> 86
<211> 274
<212> PRT
<213> Artificial Sequence

<220>
<223> 741

<400> 86
Val Asn Arg Thr Ala Phe Cys Cys Leu Ser Leu Thr Thr Ala Leu Ile
1 5 10 15

Leu Thr Ala Cys Ser Ser Gly Gly Gly Gly Val Ala Ala Asp Ile Gly
20 25 30

Ala Gly Leu Ala Asp Ala Leu Thr Ala Pro Leu Asp His Lys Asp Lys
35 40 45

Gly Leu Gln Ser Leu Thr Leu Asp Gln Ser Val Arg Lys Asn Glu Lys
50 55 60

Leu Lys Leu Ala Ala Gln Gly Ala Glu Lys Thr Tyr Gly Asn Gly Asp
65 70 75 80

Ser Leu Asn Thr Gly Lys Leu Lys Asn Asp Lys Val Ser Arg Phe Asp
85 90 95

Phe Ile Arg Gln Ile Glu Val Asp Gly Gln Leu Ile Thr Leu Glu Ser
100 105 110

Gly Glu Phe Gln Val Tyr Lys Gln Ser His Ser Ala Leu Thr Ala Phe
115 120 125

Gln Thr Glu Gln Ile Gln Asp Ser Glu His Ser Gly Lys Met Val Ala
130 135 140

Lys Arg Gln Phe Arg Ile Gly Asp Ile Ala Gly Glu His Thr Ser Phe
145 150 155 160

Asp Lys Leu Pro Glu Gly Gly Arg Ala Thr Tyr Arg Gly Thr Ala Phe
165 170 175

Gly Ser Asp Asp Ala Gly Gly Lys Leu Thr Tyr Thr Ile Asp Phe Ala
180 185 190

Ala Lys Gln Gly Asn Gly Lys Ile Glu His Leu Lys Ser Pro Glu Leu
195 200 205

Asn Val Asp Leu Ala Ala Ala Asp Ile Lys Pro Asp Gly Lys Arg His
210 215 220

Ala Val Ile Ser Gly Ser Val Leu Tyr Asn Gln Ala Glu Lys Gly Ser
225 230 235 240

Tyr Ser Leu Gly Ile Phe Gly Gly Lys Ala Gln Glu Val Ala Gly Ser
245 250 255

Ala Glu Val Lys Thr Val Asn Gly Ile Arg His Ile Gly Leu Ala Ala
260 265 270

Lys Gln

<210> 87
<211> 1082

<212> PRT
<213> Artificial Sequence

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<400> 87

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Met Ala Leu Ala Val Ala Thr Thr Leu Ser Ala Cys Leu Gly Gly Gly
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Gly Gly Gly Thr Ser Ala Pro Asp Phe Asn Ala Gly Gly Thr Gly Ile
        35                  40                  45

Gly Ser Asn Ser Arg Ala Thr Thr Ala Lys Ser Ala Ala Val Ser Tyr
    50                  55                  60

Ala Gly Ile Lys Asn Glu Met Cys Lys Asp Arg Ser Met Leu Cys Ala
65                  70                  75                  80

Gly Arg Asp Asp Val Ala Val Thr Asp Arg Asp Ala Lys Ile Asn Ala
                85                  90                  95

Pro Pro Pro Asn Leu His Thr Gly Asp Phe Pro Asn Pro Asn Asp Ala
            100                 105                 110

Tyr Lys Asn Leu Ile Asn Leu Lys Pro Ala Ile Glu Ala Gly Tyr Thr
        115                 120                 125

Gly Arg Gly Val Glu Val Gly Ile Val Asp Thr Gly Glu Ser Val Gly
    130                 135                 140

Ser Ile Ser Phe Pro Glu Leu Tyr Gly Arg Lys Glu His Gly Tyr Asn
145                 150                 155                 160

Glu Asn Tyr Lys Asn Tyr Thr Ala Tyr Met Arg Lys Glu Ala Pro Glu
                165                 170                 175

Asp Gly Gly Gly Lys Asp Ile Glu Ala Ser Phe Asp Asp Glu Ala Val
            180                 185                 190

Ile Glu Thr Glu Ala Lys Pro Thr Asp Ile Arg His Val Lys Glu Ile
        195                 200                 205

Gly His Ile Asp Leu Val Ser His Ile Ile Gly Gly Arg Ser Val Asp
    210                 215                 220

Gly Arg Pro Ala Gly Gly Ile Ala Pro Asp Ala Thr Leu His Ile Met
225                 230                 235                 240

Asn Thr Asn Asp Glu Thr Lys Asn Glu Met Met Val Ala Ala Ile Arg
                245                 250                 255

Asn Ala Trp Val Lys Leu Gly Glu Arg Gly Val Arg Ile Val Asn Asn
            260                 265                 270

Ser Phe Gly Thr Thr Ser Arg Ala Gly Thr Ala Asp Leu Phe Gln Ile
        275                 280                 285

Ala Asn Ser Glu Glu Gln Tyr Arg Gln Ala Leu Leu Asp Tyr Ser Gly
    290                 295                 300

Gly Asp Lys Thr Asp Glu Gly Ile Arg Leu Met Gln Gln Ser Asp Tyr
305                 310                 315                 320

Gly Asn Leu Ser Tyr His Ile Arg Asn Lys Asn Met Leu Phe Ile Phe
                325                 330                 335
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Ser Thr Gly Asn Asp Ala Gln Ala Gln Pro Asn Thr Tyr Ala Leu Leu
            340                 345                 350

Pro Phe Tyr Glu Lys Asp Ala Gln Lys Gly Ile Ile Thr Val Ala Gly
        355                 360                 365

Val Asp Arg Ser Gly Glu Lys Phe Lys Arg Glu Met Tyr Gly Glu Pro
    370                 375                 380

Gly Thr Glu Pro Leu Glu Tyr Gly Ser Asn His Cys Gly Ile Thr Ala
385                 390                 395                 400

Met Trp Cys Leu Ser Ala Pro Tyr Glu Ala Ser Val Arg Phe Thr Arg
                405                 410                 415

Thr Asn Pro Ile Gln Ile Ala Gly Thr Ser Phe Ser Ala Pro Ile Val
            420                 425                 430

Thr Gly Thr Ala Ala Leu Leu Leu Gln Lys Tyr Pro Trp Met Ser Asn
        435                 440                 445

Asp Asn Leu Arg Thr Thr Leu Leu Thr Thr Ala Gln Asp Ile Gly Ala
    450                 455                 460

Val Gly Val Asp Ser Lys Phe Gly Trp Gly Leu Leu Asp Ala Gly Lys
465                 470                 475                 480

Ala Met Asn Gly Pro Ala Ser Phe Pro Phe Gly Asp Phe Thr Ala Asp
                485                 490                 495

Thr Lys Gly Thr Ser Asp Ile Ala Tyr Ser Phe Arg Asn Asp Ile Ser
            500                 505                 510

Gly Thr Gly Gly Leu Ile Lys Lys Gly Gly Ser Gln Leu Gln Leu His
        515                 520                 525

Gly Asn Asn Thr Tyr Thr Gly Lys Thr Ile Ile Glu Gly Gly Ser Leu
    530                 535                 540

Val Leu Tyr Gly Asn Asn Lys Ser Asp Met Arg Val Glu Thr Lys Gly
545                 550                 555                 560

Ala Leu Ile Tyr Asn Gly Ala Ala Ser Gly Gly Ser Leu Asn Ser Asp
                565                 570                 575

Gly Ile Val Tyr Leu Ala Asp Thr Asp Gln Ser Gly Ala Asn Glu Thr
            580                 585                 590

Val His Ile Lys Gly Ser Leu Gln Leu Asp Gly Lys Gly Thr Leu Tyr
        595                 600                 605

Thr Arg Leu Gly Lys Leu Leu Lys Val Asp Gly Thr Ala Ile Ile Gly
    610                 615                 620

Gly Lys Leu Tyr Met Ser Ala Arg Gly Lys Gly Ala Gly Tyr Leu Asn
625                 630                 635                 640

Ser Thr Gly Arg Arg Val Pro Phe Leu Ser Ala Ala Lys Ile Gly Gln
                645                 650                 655

Asp Tyr Ser Phe Phe Thr Asn Ile Glu Thr Asp Gly Gly Leu Leu Ala
            660                 665                 670

Ser Leu Asp Ser Val Glu Lys Thr Ala Gly Ser Glu Gly Asp Thr Leu
        675                 680                 685

Ser Tyr Tyr Val Arg Arg Gly Asn Ala Ala Arg Thr Ala Ser Ala Ala
    690                 695                 700
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Ala His Ser Ala Pro Ala Gly Leu Lys His Ala Val Glu Gln Gly Gly
705 710 715 720

Ser Asn Leu Glu Asn Leu Met Val Glu Leu Asp Ala Ser Glu Ser Ser
725 730 735

Ala Thr Pro Glu Thr Val Glu Thr Ala Ala Ala Asp Arg Thr Asp Met
740 745 750

Pro Gly Ile Arg Pro Tyr Gly Ala Thr Phe Arg Ala Ala Ala Ala Val
755 760 765

Gln His Ala Asn Ala Ala Asp Gly Val Arg Ile Phe Asn Ser Leu Ala
770 775 780

Ala Thr Val Tyr Ala Asp Ser Thr Ala Ala His Ala Asp Met Gln Gly
785 790 795 800

Arg Arg Leu Lys Ala Val Ser Asp Gly Leu Asp His Asn Gly Thr Gly
805 810 815

Leu Arg Val Ile Ala Gln Thr Gln Gln Asp Gly Gly Thr Trp Glu Gln
820 825 830

Gly Gly Val Glu Gly Lys Met Arg Gly Ser Thr Gln Thr Val Gly Ile
835 840 845

Ala Ala Lys Thr Gly Glu Asn Thr Thr Ala Ala Ala Thr Leu Gly Met
850 855 860

Gly Arg Ser Thr Trp Ser Glu Asn Ser Ala Asn Ala Lys Thr Asp Ser
865 870 875 880

Ile Ser Leu Phe Ala Gly Ile Arg His Asp Ala Gly Asp Ile Gly Tyr
885 890 895

Leu Lys Gly Leu Phe Ser Tyr Gly Arg Tyr Lys Asn Ser Ile Ser Arg
900 905 910

Ser Thr Gly Ala Asp Glu His Ala Glu Gly Ser Val Asn Gly Thr Leu
915 920 925

Met Gln Leu Gly Ala Leu Gly Gly Val Asn Val Pro Phe Ala Ala Thr
930 935 940

Gly Asp Leu Thr Val Glu Gly Gly Leu Arg Tyr Asp Leu Leu Lys Gln
945 950 955 960

Asp Ala Phe Ala Glu Lys Gly Ser Ala Leu Gly Trp Ser Gly Asn Ser
965 970 975

Leu Thr Glu Gly Thr Leu Val Gly Leu Ala Gly Leu Lys Leu Ser Gln
980 985 990

Pro Leu Ser Asp Lys Ala Val Leu Phe Ala Thr Ala Gly Val Glu Arg
995 1000 1005

Asp Leu Asn Gly Arg Asp Tyr Thr Val Thr Gly Gly Phe Thr Gly Ala
1010 1015 1020

Thr Ala Ala Thr Gly Lys Thr Gly Ala Arg Asn Met Pro His Thr Arg
1025 1030 1035 1040

Leu Val Ala Gly Leu Gly Ala Asp Val Glu Phe Gly Asn Gly Trp Asn
1045 1050 1055

Gly Leu Ala Arg Tyr Ser Tyr Ala Gly Ser Lys Gln Tyr Gly Asn His
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Ser Gly Arg Val Gly Val Gly Tyr Arg Phe
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<210> 88
<211> 2505
<212> DNA
<213> Artificial Sequence

<220>
<223> deltaG287-919

<400> 88
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<211> 832
<212> PRT
<213> Artificial Sequence

<220>
<223> deltaG287-919

<400> 89
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Ala Pro Val Val Ala Glu Lys Glu Thr Glu Val Lys Glu Asp Ala Pro

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Gln Ala Gly Ser Gln Gly Gln Gly Ala Pro Ser Thr Gln Gly Ser Gln
35 40 45

Asp Met Ala Ala Val Ser Ala Glu Asn Thr Gly Asn Gly Gly Ala Ala
50 55 60

Thr Thr Asp Lys Pro Lys Asn Glu Asp Glu Gly Pro Gln Asn Asp Met
65 70 75 80

Pro Gln Asn Ser Ala Glu Ser Ala Asn Gln Thr Gly Asn Asn Gln Pro
85 90 95

Ala Asp Ser Ser Asp Ser Ala Pro Ala Ser Asn Pro Ala Pro Ala Asn
100 105 110

Gly Gly Ser Asn Phe Gly Arg Val Asp Leu Ala Asn Gly Val Leu Ile
115 120 125

Asp Gly Pro Ser Gln Asn Ile Thr Leu Thr His Cys Lys Gly Asp Ser
130 135 140

Cys Asn Gly Asp Asn Leu Leu Asp Glu Glu Ala Pro Ser Lys Ser Glu
145 150 155 160

Phe Glu Asn Leu Asn Glu Ser Glu Arg Ile Glu Lys Tyr Lys Lys Asp
165 170 175

Gly Lys Ser Asp Lys Phe Thr Asn Leu Val Ala Thr Ala Val Gln Ala
180 185 190

Asn Gly Thr Asn Lys Tyr Val Ile Ile Tyr Lys Asp Lys Ser Ala Ser
195 200 205

Ser Ser Ser Ala Arg Phe Arg Arg Ser Ala Arg Ser Arg Arg Ser Leu
210 215 220

Pro Ala Glu Met Pro Leu Ile Pro Val Asn Gln Ala Asp Thr Leu Ile
225 230 235 240

Val Asp Gly Glu Ala Val Ser Leu Thr Gly His Ser Gly Asn Ile Phe
245 250 255

Ala Pro Glu Gly Asn Tyr Arg Tyr Leu Thr Tyr Gly Ala Glu Lys Leu
260 265 270

Pro Gly Gly Ser Tyr Ala Leu Arg Val Gln Gly Glu Pro Ala Lys Gly
275 280 285

Glu Met Leu Ala Gly Thr Ala Val Tyr Asn Gly Glu Val Leu His Phe
290 295 300

His Thr Glu Asn Gly Arg Pro Tyr Pro Thr Arg Gly Arg Phe Ala Ala
305 310 315 320

Lys Val Asp Phe Gly Ser Lys Ser Val Asp Gly Ile Ile Asp Ser Gly
325 330 335

Asp Asp Leu His Met Gly Thr Gln Lys Phe Lys Ala Ala Ile Asp Gly
340 345 350

Asn Gly Phe Lys Gly Thr Trp Thr Glu Asn Gly Gly Gly Asp Val Ser
355 360 365

Gly Arg Phe Tyr Gly Pro Ala Gly Glu Glu Val Ala Gly Lys Tyr Ser
370 375 380

Tyr Arg Pro Thr Asp Ala Glu Lys Gly Gly Phe Gly Val Phe Ala Gly

385 390 395 400

Lys Lys Glu Gln Asp Gly Ser Gly Gly Gly Gly Cys Gln Ser Lys Ser
405 410 415

Ile Gln Thr Phe Pro Gln Pro Asp Thr Ser Val Ile Asn Gly Pro Asp
420 425 430

Arg Pro Val Gly Ile Pro Asp Pro Ala Gly Thr Thr Val Gly Gly Gly
435 440 445

Gly Ala Val Tyr Thr Val Val Pro His Leu Ser Leu Pro His Trp Ala
450 455 460

Ala Gln Asp Phe Ala Lys Ser Leu Gln Ser Phe Arg Leu Gly Cys Ala
465 470 475 480

Asn Leu Lys Asn Arg Gln Gly Trp Gln Asp Val Cys Ala Gln Ala Phe
485 490 495

Gln Thr Pro Val His Ser Phe Gln Ala Lys Gln Phe Phe Glu Arg Tyr
500 505 510

Phe Thr Pro Trp Gln Val Ala Gly Asn Gly Ser Leu Ala Gly Thr Val
515 520 525

Thr Gly Tyr Tyr Glu Pro Val Leu Lys Gly Asp Asp Arg Arg Thr Ala
530 535 540

Gln Ala Arg Phe Pro Ile Tyr Gly Ile Pro Asp Asp Phe Ile Ser Val
545 550 555 560

Pro Leu Pro Ala Gly Leu Arg Ser Gly Lys Ala Leu Val Arg Ile Arg
565 570 575

Gln Thr Gly Lys Asn Ser Gly Thr Ile Asp Asn Thr Gly Gly Thr His
580 585 590

Thr Ala Asp Leu Ser Arg Phe Pro Ile Thr Ala Arg Thr Thr Ala Ile
595 600 605

Lys Gly Arg Phe Glu Gly Ser Arg Phe Leu Pro Tyr His Thr Arg Asn
610 615 620

Gln Ile Asn Gly Gly Ala Leu Asp Gly Lys Ala Pro Ile Leu Gly Tyr
625 630 635 640

Ala Glu Asp Pro Val Glu Leu Phe Phe Met His Ile Gln Gly Ser Gly
645 650 655

Arg Leu Lys Thr Pro Ser Gly Lys Tyr Ile Arg Ile Gly Tyr Ala Asp
660 665 670

Lys Asn Glu His Pro Tyr Val Ser Ile Gly Arg Tyr Met Ala Asp Lys
675 680 685

Gly Tyr Leu Lys Leu Gly Gln Thr Ser Met Gln Gly Ile Lys Ala Tyr
690 695 700

Met Arg Gln Asn Pro Gln Arg Leu Ala Glu Val Leu Gly Gln Asn Pro
705 710 715 720

Ser Tyr Ile Phe Phe Arg Glu Leu Ala Gly Ser Ser Asn Asp Gly Pro
725 730 735

Val Gly Ala Leu Gly Thr Pro Leu Met Gly Glu Tyr Ala Gly Ala Val
740 745 750

Asp Arg His Tyr Ile Thr Leu Gly Ala Pro Leu Phe Val Ala Thr Ala

755 760 765

His Pro Val Thr Arg Lys Ala Leu Asn Arg Leu Ile Met Ala Gln Asp
770 775 780

Thr Gly Ser Ala Ile Lys Gly Ala Val Arg Val Asp Tyr Phe Trp Gly
785 790 795 800

Tyr Gly Asp Glu Ala Gly Glu Leu Ala Gly Lys Gln Lys Thr Thr Gly
805 810 815

Tyr Val Trp Gln Leu Leu Pro Asn Gly Met Lys Pro Glu Tyr Arg Pro
820 825 830

<210> 90
<211> 1746
<212> DNA
<213> Artificial Sequence

<220>
<223> deltaG287-953

<400> 90
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ggcggtgcgg caacaacgga caaacccaaa aatgaagacg agggaccgca aaatgatatg    240
ccgcaaaatt ccgccgaatc cgcaaatcaa acagggaaca accaacccgc cgattcttca    300
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tgcggcggcg acttcagcac caccatcgac cgcaccaaat ggggcgtgga ctacctcgtt   1680
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<210> 91
<211> 579
<212> PRT
<213> Artificial Sequence

<220>
<223> deltaG287-953

<400> 91
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Gln Ala Gly Ser Gln Gly Gln Gly Ala Pro Ser Thr Gln Gly Ser Gln
        35                  40                  45

Asp Met Ala Ala Val Ser Ala Glu Asn Thr Gly Asn Gly Gly Ala Ala
    50                  55                  60

Thr Thr Asp Lys Pro Lys Asn Glu Asp Glu Gly Pro Gln Asn Asp Met
65                  70                  75                  80

Pro Gln Asn Ser Ala Glu Ser Ala Asn Gln Thr Gly Asn Asn Gln Pro
                85                  90                  95

Ala Asp Ser Ser Asp Ser Ala Pro Ala Ser Asn Pro Ala Pro Ala Asn
            100                 105                 110

Gly Gly Ser Asn Phe Gly Arg Val Asp Leu Ala Asn Gly Val Leu Ile
        115                 120                 125

Asp Gly Pro Ser Gln Asn Ile Thr Leu Thr His Cys Lys Gly Asp Ser
    130                 135                 140

Cys Asn Gly Asp Asn Leu Leu Asp Glu Glu Ala Pro Ser Lys Ser Glu
145                 150                 155                 160

Phe Glu Asn Leu Asn Glu Ser Glu Arg Ile Glu Lys Tyr Lys Lys Asp
                165                 170                 175

Gly Lys Ser Asp Lys Phe Thr Asn Leu Val Ala Thr Ala Val Gln Ala
            180                 185                 190

Asn Gly Thr Asn Lys Tyr Val Ile Ile Tyr Lys Asp Lys Ser Ala Ser
        195                 200                 205

Ser Ser Ser Ala Arg Phe Arg Arg Ser Ala Arg Ser Arg Arg Ser Leu
    210                 215                 220

Pro Ala Glu Met Pro Leu Ile Pro Val Asn Gln Ala Asp Thr Leu Ile
225                 230                 235                 240

Val Asp Gly Glu Ala Val Ser Leu Thr Gly His Ser Gly Asn Ile Phe
                245                 250                 255

Ala Pro Glu Gly Asn Tyr Arg Tyr Leu Thr Tyr Gly Ala Glu Lys Leu
            260                 265                 270

Pro Gly Gly Ser Tyr Ala Leu Arg Val Gln Gly Glu Pro Ala Lys Gly
        275                 280                 285

Glu Met Leu Ala Gly Thr Ala Val Tyr Asn Gly Glu Val Leu His Phe
    290                 295                 300

His Thr Glu Asn Gly Arg Pro Tyr Pro Thr Arg Gly Arg Phe Ala Ala
305                 310                 315                 320

Lys Val Asp Phe Gly Ser Lys Ser Val Asp Gly Ile Ile Asp Ser Gly
                325                 330                 335

Asp Asp Leu His Met Gly Thr Gln Lys Phe Lys Ala Ala Ile Asp Gly
            340                 345                 350

Asn Gly Phe Lys Gly Thr Trp Thr Glu Asn Gly Gly Gly Asp Val Ser
        355                 360                 365

Gly Arg Phe Tyr Gly Pro Ala Gly Glu Glu Val Ala Gly Lys Tyr Ser
    370                 375                 380

Tyr Arg Pro Thr Asp Ala Glu Lys Gly Gly Phe Gly Val Phe Ala Gly
385                 390                 395                 400
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Lys Lys Glu Gln Asp Gly Ser Gly Gly Gly Gly Ala Thr Tyr Lys Val
405 410 415

Asp Glu Tyr His Ala Asn Ala Arg Phe Ala Ile Asp His Phe Asn Thr
420 425 430

Ser Thr Asn Val Gly Gly Phe Tyr Gly Leu Thr Gly Ser Val Glu Phe
435 440 445

Asp Gln Ala Lys Arg Asp Gly Lys Ile Asp Ile Thr Ile Pro Val Ala
450 455 460

Asn Leu Gln Ser Gly Ser Gln His Phe Thr Asp His Leu Lys Ser Ala
465 470 475 480

Asp Ile Phe Asp Ala Ala Gln Tyr Pro Asp Ile Arg Phe Val Ser Thr
485 490 495

Lys Phe Asn Phe Asn Gly Lys Lys Leu Val Ser Val Asp Gly Asn Leu
500 505 510

Thr Met His Gly Lys Thr Ala Pro Val Lys Leu Lys Ala Glu Lys Phe
515 520 525

Asn Cys Tyr Gln Ser Pro Met Ala Lys Thr Glu Val Cys Gly Gly Asp
530 535 540

Phe Ser Thr Thr Ile Asp Arg Thr Lys Trp Gly Val Asp Tyr Leu Val
545 550 555 560

Asn Val Gly Met Thr Lys Ser Val Arg Ile Asp Ile Gln Ile Glu Ala
565 570 575

Ala Lys Gln

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<211> 2388
<212> DNA
<213> Artificial Sequence

<220>
<223> deltaG287-961

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gctggagaga ccatctacga cattgatgaa gacggcacaa ttaccaaaaa agacgcaact 1380

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gatgccgctc tggatgcaac caccaacgcc ttgaataaat tgggagaaaa tataacgaca    1620
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<210> 93
<211> 793
<212> PRT
<213> Artificial Sequence

<220>
<223> deltaG287-961

<400> 93

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Ala Pro Val Val Ala Glu Lys Glu Thr Glu Val Lys Glu Asp Ala Pro
            20                  25                  30

Gln Ala Gly Ser Gln Gly Gln Gly Ala Pro Ser Thr Gln Gly Ser Gln
        35                  40                  45

Asp Met Ala Ala Val Ser Ala Glu Asn Thr Gly Asn Gly Gly Ala Ala
    50                  55                  60

Thr Thr Asp Lys Pro Lys Asn Glu Asp Glu Gly Pro Gln Asn Asp Met
65                  70                  75                  80

Pro Gln Asn Ser Ala Glu Ser Ala Asn Gln Thr Gly Asn Asn Gln Pro
                85                  90                  95

Ala Asp Ser Ser Asp Ser Ala Pro Ala Ser Asn Pro Ala Pro Ala Asn
            100                 105                 110

Gly Gly Ser Asn Phe Gly Arg Val Asp Leu Ala Asn Gly Val Leu Ile
        115                 120                 125

Asp Gly Pro Ser Gln Asn Ile Thr Leu Thr His Cys Lys Gly Asp Ser
    130                 135                 140

Cys Asn Gly Asp Asn Leu Leu Asp Glu Glu Ala Pro Ser Lys Ser Glu
145                 150                 155                 160

Phe Glu Asn Leu Asn Glu Ser Glu Arg Ile Glu Lys Tyr Lys Lys Asp
                165                 170                 175

Gly Lys Ser Asp Lys Phe Thr Asn Leu Val Ala Thr Ala Val Gln Ala
            180                 185                 190

Asn Gly Thr Asn Lys Tyr Val Ile Ile Tyr Lys Asp Lys Ser Ala Ser
        195                 200                 205

Ser Ser Ser Ala Arg Phe Arg Arg Ser Ala Arg Ser Arg Arg Ser Leu
    210                 215                 220
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Pro Ala Glu Met Pro Leu Ile Pro Val Asn Gln Ala Asp Thr Leu Ile
225                 230                 235                 240

Val Asp Gly Glu Ala Val Ser Leu Thr Gly His Ser Gly Asn Ile Phe
                245                 250                 255

Ala Pro Glu Gly Asn Tyr Arg Tyr Leu Thr Tyr Gly Ala Glu Lys Leu
            260                 265                 270

Pro Gly Gly Ser Tyr Ala Leu Arg Val Gln Gly Glu Pro Ala Lys Gly
        275                 280                 285

Glu Met Leu Ala Gly Thr Ala Val Tyr Asn Gly Glu Val Leu His Phe
    290                 295                 300

His Thr Glu Asn Gly Arg Pro Tyr Pro Thr Arg Gly Arg Phe Ala Ala
305                 310                 315                 320

Lys Val Asp Phe Gly Ser Lys Ser Val Asp Gly Ile Ile Asp Ser Gly
                325                 330                 335

Asp Asp Leu His Met Gly Thr Gln Lys Phe Lys Ala Ala Ile Asp Gly
            340                 345                 350

Asn Gly Phe Lys Gly Thr Trp Thr Glu Asn Gly Gly Gly Asp Val Ser
        355                 360                 365

Gly Arg Phe Tyr Gly Pro Ala Gly Glu Glu Val Ala Gly Lys Tyr Ser
    370                 375                 380

Tyr Arg Pro Thr Asp Ala Glu Lys Gly Gly Phe Gly Val Phe Ala Gly
385                 390                 395                 400

Lys Lys Glu Gln Asp Gly Ser Gly Gly Gly Gly Ala Thr Asn Asp Asp
                405                 410                 415

Asp Val Lys Lys Ala Ala Thr Val Ala Ile Ala Ala Ala Tyr Asn Asn
            420                 425                 430

Gly Gln Glu Ile Asn Gly Phe Lys Ala Gly Glu Thr Ile Tyr Asp Ile
        435                 440                 445

Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp Ala Thr Ala Ala Asp Val
    450                 455                 460

Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu Lys Lys Val Val Thr Asn
465                 470                 475                 480

Leu Thr Lys Thr Val Asn Glu Asn Lys Gln Asn Val Asp Ala Lys Val
                485                 490                 495

Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu Thr Thr Lys Leu Ala Asp
            500                 505                 510

Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala Ala Leu Asp Ala Thr Thr
        515                 520                 525

Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile Thr Thr Phe Ala Glu Glu
    530                 535                 540

Thr Lys Thr Asn Ile Val Lys Ile Asp Glu Lys Leu Glu Ala Val Ala
545                 550                 555                 560

Asp Thr Val Asp Lys His Ala Glu Ala Phe Asn Asp Ile Ala Asp Ser
                565                 570                 575

Leu Asp Glu Thr Asn Thr Lys Ala Asp Glu Ala Val Lys Thr Ala Asn
            580                 585                 590
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Glu Ala Lys Gln Thr Ala Glu Glu Thr Lys Gln Asn Val Asp Ala Lys
        595                 600                 605

Val Lys Ala Ala Glu Thr Ala Ala Gly Lys Ala Glu Ala Ala Ala Gly
    610                 615                 620

Thr Ala Asn Thr Ala Ala Asp Lys Ala Glu Ala Val Ala Ala Lys Val
625                 630                 635                 640

Thr Asp Ile Lys Ala Asp Ile Ala Thr Asn Lys Asp Asn Ile Ala Lys
                645                 650                 655

Lys Ala Asn Ser Ala Asp Val Tyr Thr Arg Glu Glu Ser Asp Ser Lys
            660                 665                 670

Phe Val Arg Ile Asp Gly Leu Asn Ala Thr Thr Glu Lys Leu Asp Thr
        675                 680                 685

Arg Leu Ala Ser Ala Glu Lys Ser Ile Ala Asp His Asp Thr Arg Leu
    690                 695                 700

Asn Gly Leu Asp Lys Thr Val Ser Asp Leu Arg Lys Glu Thr Arg Gln
705                 710                 715                 720

Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly Leu Phe Gln Pro Tyr Asn
                725                 730                 735

Val Gly Arg Phe Asn Val Thr Ala Ala Val Gly Gly Tyr Lys Ser Glu
            740                 745                 750

Ser Ala Val Ala Ile Gly Thr Gly Phe Arg Phe Thr Glu Asn Phe Ala
        755                 760                 765

Ala Lys Ala Gly Val Ala Val Gly Thr Ser Ser Gly Ser Ser Ala Ala
    770                 775                 780

Tyr His Val Gly Val Asn Tyr Glu Trp
785                 790
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<210> 94
<211> 2700
<212> DNA
<213> Artificial Sequence

<220>
<223> deltaG287NZ-919

<400> 94

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gcgccatccg cacaaggcgg tcaagatatg gcggcggttt cggaagaaaa tacaggcaat    180
ggcggtgcgg cagcaacgga caaacccaaa aatgaagacg agggggcgca aaatgatatg    240
ccgcaaaatg ccgccgatac agatagtttg acaccgaatc acaccccggc ttcgaatatg    300
ccggccggaa atatggaaaa ccaagcaccg gatgccgggg aatcggagca gccggcaaac    360
caaccggata tggcaaatac ggcggacgga atgcagggtg acgatccgtc ggcaggcggg    420
gaaaatgccg gcaatacggc tgcccaaggt acaaatcaag ccgaaaacaa tcaaaccgcc    480
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ggaaggacga acgtgggcaa ttctgttgtg attgacgggc cgtcgcaaaa tataacgttg    600
acccactgta aaggcgattc ttgtagtggc aataatttct tggatgaaga agtacagcta    660
aaatcagaat ttgaaaaatt aagtgatgca gacaaaataa gtaattacaa gaaagatggg    720
aagaatgacg ggaagaatga taaatttgtc ggtttggttg ccgatagtgt gcagatgaag    780
ggaatcaatc aatatattat cttttataaa cctaaaccca cttcatttgc gcgatttagg    840
cgttctgcac ggtcgaggcg gtcgcttccg gccgagatgc cgctgattcc cgtcaatcag    900
gcggatacgc tgattgtcga tggggaagcg gtcagcctga cggggcattc cggcaatatc    960
ttcgcgcccg aagggaatta ccggtatctg acttacgggg cggaaaaatt gcccggcgga   1020
tcgtatgccc tccgtgttca aggcgaacct tcaaaaggcg aaatgctcgc gggcacggca   1080
gtgtacaacg gcgaagtgct gcattttcat acggaaaacg gccgtccgtc cccgtccaga   1140
ggcaggtttg ccgcaaaagt cgatttcggc agcaaatctg tggacggcat tatcgacagc   1200
ggcgatggtt tgcatatggg tacgcaaaaa ttcaaagccg ccatcgatgg aaacggcttt   1260
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gattattttt ggggatacgg cgacgaagcc ggcgaacttg ccggcaaaca gaaaaccacg 2640
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<210> 95
<211> 897
<212> PRT
<213> Artificial Sequence

<220>
<223> deltaG287NZ-919

<400> 95
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Ala Pro Val Val Ser Glu Lys Glu Thr Glu Ala Lys Glu Asp Ala Pro
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Gln Ala Gly Ser Gln Gly Gln Gly Ala Pro Ser Ala Gln Gly Gly Gln
35 40 45

Asp Met Ala Ala Val Ser Glu Glu Asn Thr Gly Asn Gly Gly Ala Ala
50 55 60

Ala Thr Asp Lys Pro Lys Asn Glu Asp Glu Gly Ala Gln Asn Asp Met
65 70 75 80

Pro Gln Asn Ala Ala Asp Thr Asp Ser Leu Thr Pro Asn His Thr Pro
85 90 95

Ala Ser Asn Met Pro Ala Gly Asn Met Glu Asn Gln Ala Pro Asp Ala
100 105 110

Gly Glu Ser Glu Gln Pro Ala Asn Gln Pro Asp Met Ala Asn Thr Ala
115 120 125

Asp Gly Met Gln Gly Asp Asp Pro Ser Ala Gly Gly Glu Asn Ala Gly
130 135 140

Asn Thr Ala Ala Gln Gly Thr Asn Gln Ala Glu Asn Asn Gln Thr Ala
145 150 155 160

Gly Ser Gln Asn Pro Ala Ser Ser Thr Asn Pro Ser Ala Thr Asn Ser
165 170 175

Gly Gly Asp Phe Gly Arg Thr Asn Val Gly Asn Ser Val Val Ile Asp
180 185 190

Gly Pro Ser Gln Asn Ile Thr Leu Thr His Cys Lys Gly Asp Ser Cys
195 200 205

Ser Gly Asn Asn Phe Leu Asp Glu Glu Val Gln Leu Lys Ser Glu Phe
210 215 220

Glu Lys Leu Ser Asp Ala Asp Lys Ile Ser Asn Tyr Lys Lys Asp Gly
225 230 235 240

Lys Asn Asp Gly Lys Asn Asp Lys Phe Val Gly Leu Val Ala Asp Ser
245 250 255

Val Gln Met Lys Gly Ile Asn Gln Tyr Ile Ile Phe Tyr Lys Pro Lys
260 265 270

Pro Thr Ser Phe Ala Arg Phe Arg Arg Ser Ala Arg Ser Arg Arg Ser
275 280 285

Leu Pro Ala Glu Met Pro Leu Ile Pro Val Asn Gln Ala Asp Thr Leu
290 295 300

Ile Val Asp Gly Glu Ala Val Ser Leu Thr Gly His Ser Gly Asn Ile
305 310 315 320

Phe Ala Pro Glu Gly Asn Tyr Arg Tyr Leu Thr Tyr Gly Ala Glu Lys
325 330 335

Leu Pro Gly Gly Ser Tyr Ala Leu Arg Val Gln Gly Glu Pro Ser Lys
340 345 350

Gly Glu Met Leu Ala Gly Thr Ala Val Tyr Asn Gly Glu Val Leu His
355 360 365

Phe His Thr Glu Asn Gly Arg Pro Ser Pro Ser Arg Gly Arg Phe Ala
370 375 380

Ala Lys Val Asp Phe Gly Ser Lys Ser Val Asp Gly Ile Ile Asp Ser
385 390 395 400

Gly Asp Gly Leu His Met Gly Thr Gln Lys Phe Lys Ala Ala Ile Asp
405 410 415

Gly Asn Gly Phe Lys Gly Thr Trp Thr Glu Asn Gly Gly Gly Asp Val
420 425 430

Ser Gly Lys Phe Tyr Gly Pro Ala Gly Glu Glu Val Ala Gly Lys Tyr
435 440 445

Ser Tyr Arg Pro Thr Asp Ala Glu Lys Gly Gly Phe Gly Val Phe Ala
450 455 460

Gly Lys Lys Glu Gln Asp Gly Ser Gly Gly Gly Gly Cys Gln Ser Lys
465 470 475 480

Ser Ile Gln Thr Phe Pro Gln Pro Asp Thr Ser Val Ile Asn Gly Pro
485 490 495

Asp Arg Pro Val Gly Ile Pro Asp Pro Ala Gly Thr Thr Val Gly Gly
500 505 510

Gly Gly Ala Val Tyr Thr Val Val Pro His Leu Ser Leu Pro His Trp
515 520 525

Ala Ala Gln Asp Phe Ala Lys Ser Leu Gln Ser Phe Arg Leu Gly Cys
530 535 540

Ala Asn Leu Lys Asn Arg Gln Gly Trp Gln Asp Val Cys Ala Gln Ala
545 550 555 560

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Phe Gln Thr Pro Val His Ser Phe Gln Ala Lys Gln Phe Phe Glu Arg
                565                 570                 575

Tyr Phe Thr Pro Trp Gln Val Ala Gly Asn Gly Ser Leu Ala Gly Thr
            580                 585                 590

Val Thr Gly Tyr Tyr Glu Pro Val Leu Lys Gly Asp Asp Arg Arg Thr
        595                 600                 605

Ala Gln Ala Arg Phe Pro Ile Tyr Gly Ile Pro Asp Asp Phe Ile Ser
    610                 615                 620

Val Pro Leu Pro Ala Gly Leu Arg Ser Gly Lys Ala Leu Val Arg Ile
625                 630                 635                 640

Arg Gln Thr Gly Lys Asn Ser Gly Thr Ile Asp Asn Thr Gly Gly Thr
                645                 650                 655

His Thr Ala Asp Leu Ser Arg Phe Pro Ile Thr Ala Arg Thr Thr Ala
            660                 665                 670

Ile Lys Gly Arg Phe Glu Gly Ser Arg Phe Leu Pro Tyr His Thr Arg
        675                 680                 685

Asn Gln Ile Asn Gly Gly Ala Leu Asp Gly Lys Ala Pro Ile Leu Gly
    690                 695                 700

Tyr Ala Glu Asp Pro Val Glu Leu Phe Phe Met His Ile Gln Gly Ser
705                 710                 715                 720

Gly Arg Leu Lys Thr Pro Ser Gly Lys Tyr Ile Arg Ile Gly Tyr Ala
                725                 730                 735

Asp Lys Asn Glu His Pro Tyr Val Ser Ile Gly Arg Tyr Met Ala Asp
            740                 745                 750

Lys Gly Tyr Leu Lys Leu Gly Gln Thr Ser Met Gln Gly Ile Lys Ala
        755                 760                 765

Tyr Met Arg Gln Asn Pro Gln Arg Leu Ala Glu Val Leu Gly Gln Asn
    770                 775                 780

Pro Ser Tyr Ile Phe Phe Arg Glu Leu Ala Gly Ser Ser Asn Asp Gly
785                 790                 795                 800

Pro Val Gly Ala Leu Gly Thr Pro Leu Met Gly Glu Tyr Ala Gly Ala
                805                 810                 815

Val Asp Arg His Tyr Ile Thr Leu Gly Ala Pro Leu Phe Val Ala Thr
            820                 825                 830

Ala His Pro Val Thr Arg Lys Ala Leu Asn Arg Leu Ile Met Ala Gln
        835                 840                 845

Asp Thr Gly Ser Ala Ile Lys Gly Ala Val Arg Val Asp Tyr Phe Trp
    850                 855                 860

Gly Tyr Gly Asp Glu Ala Gly Glu Leu Ala Gly Lys Gln Lys Thr Thr
865                 870                 875                 880

Gly Tyr Val Trp Gln Leu Leu Pro Asn Gly Met Lys Pro Glu Tyr Arg
                885                 890                 895

Pro
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<210> 96
<211> 1941

<212> DNA
<213> Artificial Sequence

<220>
<223> deltaG287NZ-953

<400> 96
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<210> 97
<211> 644
<212> PRT
<213> Artificial Sequence

<220>
<223> deltaG287NZ-953

<400> 97
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Ala Pro Val Val Ser Glu Lys Glu Thr Glu Ala Lys Glu Asp Ala Pro
20 25 30

Gln Ala Gly Ser Gln Gly Gln Gly Ala Pro Ser Ala Gln Gly Gly Gln
35 40 45

Asp Met Ala Ala Val Ser Glu Glu Asn Thr Gly Asn Gly Gly Ala Ala
50 55 60

Ala Thr Asp Lys Pro Lys Asn Glu Asp Glu Gly Ala Gln Asn Asp Met
65 70 75 80

Pro Gln Asn Ala Ala Asp Thr Asp Ser Leu Thr Pro Asn His Thr Pro
85 90 95

Ala Ser Asn Met Pro Ala Gly Asn Met Glu Asn Gln Ala Pro Asp Ala

100 105 110

Gly Glu Ser Glu Gln Pro Ala Asn Gln Pro Asp Met Ala Asn Thr Ala
115 120 125

Asp Gly Met Gln Gly Asp Asp Pro Ser Ala Gly Gly Glu Asn Ala Gly
130 135 140

Asn Thr Ala Ala Gln Gly Thr Asn Gln Ala Glu Asn Asn Gln Thr Ala
145 150 155 160

Gly Ser Gln Asn Pro Ala Ser Ser Thr Asn Pro Ser Ala Thr Asn Ser
165 170 175

Gly Gly Asp Phe Gly Arg Thr Asn Val Gly Asn Ser Val Val Ile Asp
180 185 190

Gly Pro Ser Gln Asn Ile Thr Leu Thr His Cys Lys Gly Asp Ser Cys
195 200 205

Ser Gly Asn Asn Phe Leu Asp Glu Glu Val Gln Leu Lys Ser Glu Phe
210 215 220

Glu Lys Leu Ser Asp Ala Asp Lys Ile Ser Asn Tyr Lys Lys Asp Gly
225 230 235 240

Lys Asn Asp Gly Lys Asn Asp Lys Phe Val Gly Leu Val Ala Asp Ser
245 250 255

Val Gln Met Lys Gly Ile Asn Gln Tyr Ile Ile Phe Tyr Lys Pro Lys
260 265 270

Pro Thr Ser Phe Ala Arg Phe Arg Arg Ser Ala Arg Ser Arg Arg Ser
275 280 285

Leu Pro Ala Glu Met Pro Leu Ile Pro Val Asn Gln Ala Asp Thr Leu
290 295 300

Ile Val Asp Gly Glu Ala Val Ser Leu Thr Gly His Ser Gly Asn Ile
305 310 315 320

Phe Ala Pro Glu Gly Asn Tyr Arg Tyr Leu Thr Tyr Gly Ala Glu Lys
325 330 335

Leu Pro Gly Gly Ser Tyr Ala Leu Arg Val Gln Gly Glu Pro Ser Lys
340 345 350

Gly Glu Met Leu Ala Gly Thr Ala Val Tyr Asn Gly Glu Val Leu His
355 360 365

Phe His Thr Glu Asn Gly Arg Pro Ser Pro Ser Arg Gly Arg Phe Ala
370 375 380

Ala Lys Val Asp Phe Gly Ser Lys Ser Val Asp Gly Ile Ile Asp Ser
385 390 395 400

Gly Asp Gly Leu His Met Gly Thr Gln Lys Phe Lys Ala Ala Ile Asp
405 410 415

Gly Asn Gly Phe Lys Gly Thr Trp Thr Glu Asn Gly Gly Gly Asp Val
420 425 430

Ser Gly Lys Phe Tyr Gly Pro Ala Gly Glu Glu Val Ala Gly Lys Tyr
435 440 445

Ser Tyr Arg Pro Thr Asp Ala Glu Lys Gly Gly Phe Gly Val Phe Ala
450 455 460

Gly Lys Lys Glu Gln Asp Gly Ser Gly Gly Gly Gly Ala Thr Tyr Lys

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465                 470                 475                 480

Val Asp Glu Tyr His Ala Asn Ala Arg Phe Ala Ile Asp His Phe Asn
                485                 490                 495

Thr Ser Thr Asn Val Gly Gly Phe Tyr Gly Leu Thr Gly Ser Val Glu
            500                 505                 510

Phe Asp Gln Ala Lys Arg Asp Gly Lys Ile Asp Ile Thr Ile Pro Val
        515                 520                 525

Ala Asn Leu Gln Ser Gly Ser Gln His Phe Thr Asp His Leu Lys Ser
    530                 535                 540

Ala Asp Ile Phe Asp Ala Ala Gln Tyr Pro Asp Ile Arg Phe Val Ser
545                 550                 555                 560

Thr Lys Phe Asn Phe Asn Gly Lys Lys Leu Val Ser Val Asp Gly Asn
                565                 570                 575

Leu Thr Met His Gly Lys Thr Ala Pro Val Lys Leu Lys Ala Glu Lys
            580                 585                 590

Phe Asn Cys Tyr Gln Ser Pro Met Ala Lys Thr Glu Val Cys Gly Gly
        595                 600                 605

Asp Phe Ser Thr Thr Ile Asp Arg Thr Lys Trp Gly Val Asp Tyr Leu
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Val Asn Val Gly Met Thr Lys Ser Val Arg Ile Asp Ile Gln Ile Glu
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Ala Ala Lys Gln


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Gln Ala Gly Ser Gln Gly Gln Gly Ala Pro Ser Ala Gln Gly Gly Gln
35 40 45

Asp Met Ala Ala Val Ser Glu Glu Asn Thr Gly Asn Gly Gly Ala Ala
50 55 60

Ala Thr Asp Lys Pro Lys Asn Glu Asp Glu Gly Ala Gln Asn Asp Met
65 70 75 80

Pro Gln Asn Ala Ala Asp Thr Asp Ser Leu Thr Pro Asn His Thr Pro
85 90 95

Ala Ser Asn Met Pro Ala Gly Asn Met Glu Asn Gln Ala Pro Asp Ala
100 105 110

Gly Glu Ser Glu Gln Pro Ala Asn Gln Pro Asp Met Ala Asn Thr Ala
115 120 125

Asp Gly Met Gln Gly Asp Asp Pro Ser Ala Gly Gly Glu Asn Ala Gly
130 135 140

Asn Thr Ala Ala Gln Gly Thr Asn Gln Ala Glu Asn Asn Gln Thr Ala
145 150 155 160

Gly Ser Gln Asn Pro Ala Ser Ser Thr Asn Pro Ser Ala Thr Asn Ser
165 170 175

Gly Gly Asp Phe Gly Arg Thr Asn Val Gly Asn Ser Val Val Ile Asp
180 185 190

Gly Pro Ser Gln Asn Ile Thr Leu Thr His Cys Lys Gly Asp Ser Cys
195 200 205

Ser Gly Asn Asn Phe Leu Asp Glu Glu Val Gln Leu Lys Ser Glu Phe

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Glu Lys Leu Ser Asp Ala Asp Lys Ile Ser Asn Tyr Lys Lys Asp Gly
225                 230                 235                 240

Lys Asn Asp Gly Lys Asn Asp Lys Phe Val Gly Leu Val Ala Asp Ser
                245                 250                 255

Val Gln Met Lys Gly Ile Asn Gln Tyr Ile Ile Phe Tyr Lys Pro Lys
            260                 265                 270

Pro Thr Ser Phe Ala Arg Phe Arg Arg Ser Ala Arg Ser Arg Arg Ser
        275                 280                 285

Leu Pro Ala Glu Met Pro Leu Ile Pro Val Asn Gln Ala Asp Thr Leu
    290                 295                 300

Ile Val Asp Gly Glu Ala Val Ser Leu Thr Gly His Ser Gly Asn Ile
305                 310                 315                 320

Phe Ala Pro Glu Gly Asn Tyr Arg Tyr Leu Thr Tyr Gly Ala Glu Lys
                325                 330                 335

Leu Pro Gly Gly Ser Tyr Ala Leu Arg Val Gln Gly Glu Pro Ser Lys
            340                 345                 350

Gly Glu Met Leu Ala Gly Thr Ala Val Tyr Asn Gly Glu Val Leu His
        355                 360                 365

Phe His Thr Glu Asn Gly Arg Pro Ser Pro Ser Arg Gly Arg Phe Ala
    370                 375                 380

Ala Lys Val Asp Phe Gly Ser Lys Ser Val Asp Gly Ile Ile Asp Ser
385                 390                 395                 400

Gly Asp Gly Leu His Met Gly Thr Gln Lys Phe Lys Ala Ala Ile Asp
                405                 410                 415

Gly Asn Gly Phe Lys Gly Thr Trp Thr Glu Asn Gly Gly Gly Asp Val
            420                 425                 430

Ser Gly Lys Phe Tyr Gly Pro Ala Gly Glu Glu Val Ala Gly Lys Tyr
        435                 440                 445

Ser Tyr Arg Pro Thr Asp Ala Glu Lys Gly Gly Phe Gly Val Phe Ala
    450                 455                 460

Gly Lys Lys Glu Gln Asp Gly Ser Gly Gly Gly Gly Ala Thr Asn Asp
465                 470                 475                 480

Asp Asp Val Lys Lys Ala Ala Thr Val Ala Ile Ala Ala Ala Tyr Asn
                485                 490                 495

Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala Gly Glu Thr Ile Tyr Asp
            500                 505                 510

Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp Ala Thr Ala Ala Asp
        515                 520                 525

Val Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu Lys Lys Val Val Thr
    530                 535                 540

Asn Leu Thr Lys Thr Val Asn Glu Asn Lys Gln Asn Val Asp Ala Lys
545                 550                 555                 560

Val Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu Thr Thr Lys Leu Ala
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Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala Ala Leu Asp Ala Thr
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580 585 590

Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile Thr Thr Phe Ala Glu
595 600 605

Glu Thr Lys Thr Asn Ile Val Lys Ile Asp Glu Lys Leu Glu Ala Val
610 615 620

Ala Asp Thr Val Asp Lys His Ala Glu Ala Phe Asn Asp Ile Ala Asp
625 630 635 640

Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp Glu Ala Val Lys Thr Ala
645 650 655

Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr Lys Gln Asn Val Asp Ala
660 665 670

Lys Val Lys Ala Ala Glu Thr Ala Ala Gly Lys Ala Glu Ala Ala Ala
675 680 685

Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala Glu Ala Val Ala Ala Lys
690 695 700

Val Thr Asp Ile Lys Ala Asp Ile Ala Thr Asn Lys Asp Asn Ile Ala
705 710 715 720

Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr Arg Glu Glu Ser Asp Ser
725 730 735

Lys Phe Val Arg Ile Asp Gly Leu Asn Ala Thr Thr Glu Lys Leu Asp
740 745 750

Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile Ala Asp His Asp Thr Arg
755 760 765

Leu Asn Gly Leu Asp Lys Thr Val Ser Asp Leu Arg Lys Glu Thr Arg
770 775 780

Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly Leu Phe Gln Pro Tyr
785 790 795 800

Asn Val Gly Arg Phe Asn Val Thr Ala Ala Val Gly Gly Tyr Lys Ser
805 810 815

Glu Ser Ala Val Ala Ile Gly Thr Gly Phe Arg Phe Thr Glu Asn Phe
820 825 830

Ala Ala Lys Ala Gly Val Ala Val Gly Thr Ser Ser Gly Ser Ser Ala
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Ala Tyr His Val Gly Val Asn Tyr Glu Trp
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<212> DNA
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<400> 101

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Ile Lys Asn Glu Met Cys Lys Asp Arg Ser Met Leu Cys Ala Gly Arg
        35                  40                  45

Asp Asp Val Ala Val Thr Asp Arg Asp Ala Lys Ile Asn Ala Pro Pro
    50                  55                  60

Pro Asn Leu His Thr Gly Asp Phe Pro Asn Pro Asn Asp Ala Tyr Lys
65                  70                  75                  80

Asn Leu Ile Asn Leu Lys Pro Ala Ile Glu Ala Gly Tyr Thr Gly Arg
                85                  90                  95

Gly Val Glu Val Gly Ile Val Asp Thr Gly Glu Ser Val Gly Ser Ile
            100                 105                 110

Ser Phe Pro Glu Leu Tyr Gly Arg Lys Glu His Gly Tyr Asn Glu Asn
        115                 120                 125

Tyr Lys Asn Tyr Thr Ala Tyr Met Arg Lys Glu Ala Pro Glu Asp Gly
    130                 135                 140

Gly Gly Lys Asp Ile Glu Ala Ser Phe Asp Asp Glu Ala Val Ile Glu
145                 150                 155                 160

Thr Glu Ala Lys Pro Thr Asp Ile Arg His Val Lys Glu Ile Gly His
                165                 170                 175

Ile Asp Leu Val Ser His Ile Ile Gly Gly Arg Ser Val Asp Gly Arg
            180                 185                 190

Pro Ala Gly Gly Ile Ala Pro Asp Ala Thr Leu His Ile Met Asn Thr
        195                 200                 205

Asn Asp Glu Thr Lys Asn Glu Met Met Val Ala Ala Ile Arg Asn Ala
    210                 215                 220

Trp Val Lys Leu Gly Glu Arg Gly Val Arg Ile Val Asn Asn Ser Phe
225                 230                 235                 240

Gly Thr Thr Ser Arg Ala Gly Thr Ala Asp Leu Phe Gln Ile Ala Asn
                245                 250                 255

Ser Glu Glu Gln Tyr Arg Gln Ala Leu Leu Asp Tyr Ser Gly Gly Asp
            260                 265                 270

Lys Thr Asp Glu Gly Ile Arg Leu Met Gln Gln Ser Asp Tyr Gly Asn
        275                 280                 285

Leu Ser Tyr His Ile Arg Asn Lys Asn Met Leu Phe Ile Phe Ser Thr
    290                 295                 300

Gly Asn Asp Ala Gln Ala Gln Pro Asn Thr Tyr Ala Leu Leu Pro Phe
305                 310                 315                 320

Tyr Glu Lys Asp Ala Gln Lys Gly Ile Ile Thr Val Ala Gly Val Asp
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Glu Pro Leu Glu Tyr Gly Ser Asn His Cys Gly Ile Thr Ala Met Trp
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Cys Leu Ser Ala Pro Tyr Glu Ala Ser Val Arg Phe Thr Arg Thr Asn
    370                 375                 380
Pro Ile Gln Ile Ala Gly Thr Ser Phe Ser Ala Pro Ile Val Thr Gly
385                 390                 395                 400
Thr Ala Ala Leu Leu Leu Gln Lys Tyr Pro Trp Met Ser Asn Asp Asn
                405                 410                 415
Leu Arg Thr Thr Leu Leu Thr Thr Ala Gln Asp Ile Gly Ala Val Gly
            420                 425                 430
Val Asp Ser Lys Phe Gly Trp Gly Leu Leu Asp Ala Gly Lys Ala Met
        435                 440                 445
Asn Gly Pro Ala Ser Phe Pro Phe Gly Asp Phe Thr Ala Asp Thr Lys
    450                 455                 460
Gly Thr Ser Asp Ile Ala Tyr Ser Phe Arg Asn Asp Ile Ser Gly Thr
465                 470                 475                 480
Gly Gly Leu Ile Lys Lys Gly Gly Ser Gln Leu Gln Leu His Gly Asn
                485                 490                 495
Asn Thr Tyr Thr Gly Lys Thr Ile Ile Glu Gly Gly Ser Leu Val Leu
            500                 505                 510
Tyr Gly Asn Asn Lys Ser Asp Met Arg Val Glu Thr Lys Gly Ala Leu
        515                 520                 525
Ile Tyr Asn Gly Ala Ala Ser Gly Gly Ser Leu Asn Ser Asp Gly Ile
    530                 535                 540
Val Tyr Leu Ala Asp Thr Asp Gln Ser Gly Ala Asn Glu Thr Val His
545                 550                 555                 560
Ile Lys Gly Ser Leu Gln Leu Asp Gly Lys Gly Thr Leu Tyr Thr Arg
                565                 570                 575
Leu Gly Lys Leu Leu Lys Val Asp Gly Thr Ala Ile Ile Gly Gly Lys
            580                 585                 590
Leu Tyr Met Ser Ala Arg Gly Lys Gly Ala Gly Tyr Leu Asn Ser Thr
        595                 600                 605
Gly Arg Arg Val Pro Phe Leu Ser Ala Ala Lys Ile Gly Gln Asp Tyr
    610                 615                 620
Ser Phe Phe Thr Asn Ile Glu Thr Asp Gly Gly Leu Leu Ala Ser Leu
625                 630                 635                 640
Asp Ser Val Glu Lys Thr Ala Gly Ser Glu Gly Asp Thr Leu Ser Tyr
                645                 650                 655
Tyr Val Arg Arg Gly Asn Ala Ala Arg Thr Ala Ser Ala Ala Ala His
            660                 665                 670
Ser Ala Pro Ala Gly Leu Lys His Ala Val Glu Gln Gly Gly Ser Asn
        675                 680                 685
Leu Glu Asn Leu Met Val Glu Leu Asp Ala Ser Glu Ser Ser Ala Thr
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690 695 700

Pro Glu Thr Val Glu Thr Ala Ala Ala Asp Arg Thr Asp Met Pro Gly
705 710 715 720

Ile Arg Pro Tyr Gly Ala Thr Phe Arg Ala Ala Ala Ala Val Gln His
725 730 735

Ala Asn Ala Ala Asp Gly Val Arg Ile Phe Asn Ser Leu Ala Ala Thr
740 745 750

Val Tyr Ala Asp Ser Thr Ala Ala His Ala Asp Met Gln Gly Arg Arg
755 760 765

Leu Lys Ala Val Ser Asp Gly Leu Asp His Asn Gly Thr Gly Leu Arg
770 775 780

Val Ile Ala Gln Thr Gln Gln Asp Gly Gly Thr Trp Glu Gln Gly Gly
785 790 795 800

Val Glu Gly Lys Met Arg Gly Ser Thr Gln Thr Val Gly Ile Ala Ala
805 810 815

Lys Thr Gly Glu Asn Thr Thr Ala Ala Ala Thr Leu Gly Met Gly Arg
820 825 830

Ser Thr Trp Ser Glu Asn Ser Ala Asn Ala Lys Thr Asp Ser Ile Ser
835 840 845

Leu Phe Ala Gly Ile Arg His Asp Ala Gly Asp Ile Gly Tyr Leu Lys
850 855 860

Gly Leu Phe Ser Tyr Gly Arg Tyr Lys Asn Ser Ile Ser Arg Ser Thr
865 870 875 880

Gly Ala Asp Glu His Ala Glu Gly Ser Val Asn Gly Thr Leu Met Gln
885 890 895

Leu Gly Ala Leu Gly Gly Val Asn Val Pro Phe Ala Ala Thr Gly Asp
900 905 910

Leu Thr Val Glu Gly Gly Leu Arg Tyr Asp Leu Leu Lys Gln Asp Ala
915 920 925

Phe Ala Glu Lys Gly Ser Ala Leu Gly Trp Ser Gly Asn Ser Leu Thr
930 935 940

Glu Gly Thr Leu Val Gly Leu Ala Gly Leu Lys Leu Ser Gln Pro Leu
945 950 955 960

Ser Asp Lys Ala Val Leu Phe Ala Thr Ala Gly Val Glu Arg Asp Leu
965 970 975

Asn Gly Arg Asp Tyr Thr Val Thr Gly Gly Phe Thr Gly Ala Thr Ala
980 985 990

Ala Thr Gly Lys Thr Gly Ala Arg Asn Met Pro His Thr Arg Leu Val
995 1000 1005

Ala Gly Leu Gly Ala Asp Val Glu Phe Gly Asn Gly Trp Asn Gly Leu
1010 1015 1020

Ala Arg Tyr Ser Tyr Ala Gly Ser Lys Gln Tyr Gly Asn His Ser Gly
1025 1030 1035 1040

Arg Val Gly Val Gly Tyr Arg Phe Leu Asp Gly Gly Gly Gly Thr Gly
1045 1050 1055

Ser Ser Asp Leu Ala Asn Asp Ser Phe Ile Arg Gln Val Leu Asp Arg

1060 1065 1070

Gln His Phe Glu Pro Asp Gly Lys Tyr His Leu Phe Gly Ser Arg Gly
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Ile Gly Tyr Ile Val Arg Phe Ser Asp His Gly His Glu Val His Ser
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Val Gly Asp Gly Phe Lys Arg Ala Thr Arg Tyr Ser Pro Glu Leu Asp
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Lys Asn Ile Ile Gly Ala Ala Gly Glu Ile Val Gly Ala Gly Asp Ala
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Val Gln Gly Ile Ser Glu Gly Ser Asn Ile Ala Val Met His Gly Leu
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Gly Leu Leu Ser Thr Glu Asn Lys Met Ala Arg Ile Asn Asp Leu Ala
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Phe Ala Asp Ala Ala Tyr Ala Lys Tyr Pro Ser Pro Tyr His Ser Arg
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<400> 103

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Asp Asp Val Ala Val Thr Asp Arg Asp Ala Lys Ile Asn Ala Pro Pro
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Pro Asn Leu His Thr Gly Asp Phe Pro Asn Pro Asn Asp Ala Tyr Lys
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Asn Leu Ile Asn Leu Lys Pro Ala Ile Glu Ala Gly Tyr Thr Gly Arg
                85                  90                  95

Gly Val Glu Val Gly Ile Val Asp Thr Gly Glu Ser Val Gly Ser Ile
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Ser Phe Pro Glu Leu Tyr Gly Arg Lys Glu His Gly Tyr Asn Glu Asn
        115                 120                 125

Tyr Lys Asn Tyr Thr Ala Tyr Met Arg Lys Glu Ala Pro Glu Asp Gly
    130                 135                 140

Gly Gly Lys Asp Ile Glu Ala Ser Phe Asp Asp Glu Ala Val Ile Glu
145                 150                 155                 160

Thr Glu Ala Lys Pro Thr Asp Ile Arg His Val Lys Glu Ile Gly His
                165                 170                 175

Ile Asp Leu Val Ser His Ile Ile Gly Gly Arg Ser Val Asp Gly Arg
            180                 185                 190

Pro Ala Gly Gly Ile Ala Pro Asp Ala Thr Leu His Ile Met Asn Thr
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Asn Asp Glu Thr Lys Asn Glu Met Met Val Ala Ala Ile Arg Asn Ala
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Gly Thr Thr Ser Arg Ala Gly Thr Ala Asp Leu Phe Gln Ile Ala Asn
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Ser Glu Glu Gln Tyr Arg Gln Ala Leu Leu Asp Tyr Ser Gly Gly Asp
            260                 265                 270

Lys Thr Asp Glu Gly Ile Arg Leu Met Gln Gln Ser Asp Tyr Gly Asn
        275                 280                 285

Leu Ser Tyr His Ile Arg Asn Lys Asn Met Leu Phe Ile Phe Ser Thr
    290                 295                 300

Gly Asn Asp Ala Gln Ala Gln Pro Asn Thr Tyr Ala Leu Leu Pro Phe
305                 310                 315                 320

Tyr Glu Lys Asp Ala Gln Lys Gly Ile Ile Thr Val Ala Gly Val Asp
                325                 330                 335

Arg Ser Gly Glu Lys Phe Lys Arg Glu Met Tyr Gly Glu Pro Gly Thr
            340                 345                 350

Glu Pro Leu Glu Tyr Gly Ser Asn His Cys Gly Ile Thr Ala Met Trp
        355                 360                 365

Cys Leu Ser Ala Pro Tyr Glu Ala Ser Val Arg Phe Thr Arg Thr Asn
    370                 375                 380

Pro Ile Gln Ile Ala Gly Thr Ser Phe Ser Ala Pro Ile Val Thr Gly
385                 390                 395                 400

Thr Ala Ala Leu Leu Leu Gln Lys Tyr Pro Trp Met Ser Asn Asp Asn
                405                 410                 415

Leu Arg Thr Thr Leu Leu Thr Thr Ala Gln Asp Ile Gly Ala Val Gly
            420                 425                 430

Val Asp Ser Lys Phe Gly Trp Gly Leu Leu Asp Ala Gly Lys Ala Met
        435                 440                 445

Asn Gly Pro Ala Ser Phe Pro Phe Gly Asp Phe Thr Ala Asp Thr Lys
    450                 455                 460

Gly Thr Ser Asp Ile Ala Tyr Ser Phe Arg Asn Asp Ile Ser Gly Thr
465                 470                 475                 480

Gly Gly Leu Ile Lys Lys Gly Gly Ser Gln Leu Gln Leu His Gly Asn
                485                 490                 495

Asn Thr Tyr Thr Gly Lys Thr Ile Ile Glu Gly Gly Ser Leu Val Leu
            500                 505                 510

Tyr Gly Asn Asn Lys Ser Asp Met Arg Val Glu Thr Lys Gly Ala Leu
        515                 520                 525

Ile Tyr Asn Gly Ala Ala Ser Gly Gly Ser Leu Asn Ser Asp Gly Ile
    530                 535                 540

Val Tyr Leu Ala Asp Thr Asp Gln Ser Gly Ala Asn Glu Thr Val His
545                 550                 555                 560

Ile Lys Gly Ser Leu Gln Leu Asp Gly Lys Gly Thr Leu Tyr Thr Arg
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Leu Gly Lys Leu Leu Lys Val Asp Gly Thr Ala Ile Ile Gly Gly Lys
            580                 585                 590
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Leu Tyr Met Ser Ala Arg Gly Lys Gly Ala Gly Tyr Leu Asn Ser Thr
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Gly Arg Arg Val Pro Phe Leu Ser Ala Ala Lys Ile Gly Gln Asp Tyr
610 615 620

Ser Phe Phe Thr Asn Ile Glu Thr Asp Gly Gly Leu Leu Ala Ser Leu
625 630 635 640

Asp Ser Val Glu Lys Thr Ala Gly Ser Glu Gly Asp Thr Leu Ser Tyr
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Tyr Val Arg Arg Gly Asn Ala Ala Arg Thr Ala Ser Ala Ala Ala His
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Ser Ala Pro Ala Gly Leu Lys His Ala Val Glu Gln Gly Gly Ser Asn
675 680 685

Leu Glu Asn Leu Met Val Glu Leu Asp Ala Ser Glu Ser Ser Ala Thr
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Pro Glu Thr Val Glu Thr Ala Ala Ala Asp Arg Thr Asp Met Pro Gly
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Ile Arg Pro Tyr Gly Ala Thr Phe Arg Ala Ala Ala Ala Val Gln His
725 730 735

Ala Asn Ala Ala Asp Gly Val Arg Ile Phe Asn Ser Leu Ala Ala Thr
740 745 750

Val Tyr Ala Asp Ser Thr Ala Ala His Ala Asp Met Gln Gly Arg Arg
755 760 765

Leu Lys Ala Val Ser Asp Gly Leu Asp His Asn Gly Thr Gly Leu Arg
770 775 780

Val Ile Ala Gln Thr Gln Gln Asp Gly Gly Thr Trp Glu Gln Gly Gly
785 790 795 800

Val Glu Gly Lys Met Arg Gly Ser Thr Gln Thr Val Gly Ile Ala Ala
805 810 815

Lys Thr Gly Glu Asn Thr Thr Ala Ala Ala Thr Leu Gly Met Gly Arg
820 825 830

Ser Thr Trp Ser Glu Asn Ser Ala Asn Ala Lys Thr Asp Ser Ile Ser
835 840 845

Leu Phe Ala Gly Ile Arg His Asp Ala Gly Asp Ile Gly Tyr Leu Lys
850 855 860

Gly Leu Phe Ser Tyr Gly Arg Tyr Lys Asn Ser Ile Ser Arg Ser Thr
865 870 875 880

Gly Ala Asp Glu His Ala Glu Gly Ser Val Asn Gly Thr Leu Met Gln
885 890 895

Leu Gly Ala Leu Gly Gly Val Asn Val Pro Phe Ala Ala Thr Gly Asp
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Leu Thr Val Glu Gly Gly Leu Arg Tyr Asp Leu Leu Lys Gln Asp Ala
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930 935 940

Glu Gly Thr Leu Val Gly Leu Ala Gly Leu Lys Leu Ser Gln Pro Leu
945 950 955 960

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Asn Gly Arg Asp Tyr Thr Val Thr Gly Gly Phe Thr Gly Ala Thr Ala
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Ala Gly Leu Gly Ala Asp Val Glu Phe Gly Asn Gly Trp Asn Gly Leu
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Ala Arg Tyr Ser Tyr Ala Gly Ser Lys Gln Tyr Gly Asn His Ser Gly
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Arg Val Gly Val Gly Tyr Arg Phe Leu Glu Gly Ser Gly Gly Gly Gly
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Val Arg Lys Asn Glu Lys Leu Lys Leu Ala Ala Gln Gly Ala Glu Lys
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Thr Tyr Gly Asn Gly Asp Ser Leu Asn Thr Gly Lys Leu Lys Asn Asp
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Lys Val Ser Arg Phe Asp Phe Ile Arg Gln Ile Glu Val Asp Gly Gln
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Leu Ile Thr Leu Glu Ser Gly Glu Phe Gln Val Tyr Lys Gln Ser His
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Ser Ala Leu Thr Ala Phe Gln Thr Glu Gln Ile Gln Asp Ser Glu His
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Ser Gly Lys Met Val Ala Lys Arg Gln Phe Arg Ile Gly Asp Ile Ala
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Gly Glu His Thr Ser Phe Asp Lys Leu Pro Glu Gly Gly Arg Ala Thr
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Tyr Thr Ile Asp Phe Ala Ala Lys Gln Gly Asn Gly Lys Ile Glu His
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Leu Lys Ser Pro Glu Leu Asn Val Asp Leu Ala Ala Ala Asp Ile Lys
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Pro Asp Gly Lys Arg His Ala Val Ile Ser Gly Ser Val Leu Tyr Asn
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Gln Ala Glu Lys Gly Ser Tyr Ser Leu Gly Ile Phe Gly Gly Lys Ala
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Gln Glu Val Ala Gly Ser Ala Glu Val Lys Thr Val Asn Gly Ile Arg
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agaattgatg gtctgaacgc tactaccgaa aaattggaca cacgcttggc ttctgctgaa   4020
aaatccattg ccgatcacga tactcgcctg aacggtttgg ataaaacagt gtcagacctg   4080
cgcaaagaaa cccgccaagg ccttgcagaa caagccgcgc tctccggtct gttccaacct   4140
tacaacgtgg gtcggttcaa tgtaacggct gcagtcggcg gctacaaatc cgaatcggca   4200
gtcgccatcg gtaccggctt ccgctttacc gaaaactttg ccgccaaagc aggcgtggca   4260
gtcggcactt cgtccggttc ttccgcagcc taccatgtcg gcgtcaatta cgagtggctc   4320
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<212>   PRT
<213>   Artificial Sequence

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Asn Ser Arg Ala Thr Thr Ala Lys Ser Ala Ala Val Ser Tyr Ala Gly
            20                  25                  30

Ile Lys Asn Glu Met Cys Lys Asp Arg Ser Met Leu Cys Ala Gly Arg
        35                  40                  45

Asp Asp Val Ala Val Thr Asp Arg Asp Ala Lys Ile Asn Ala Pro Pro
    50                  55                  60

Pro Asn Leu His Thr Gly Asp Phe Pro Asn Pro Asn Asp Ala Tyr Lys
65                  70                  75                  80

Asn Leu Ile Asn Leu Lys Pro Ala Ile Glu Ala Gly Tyr Thr Gly Arg
                85                  90                  95

Gly Val Glu Val Gly Ile Val Asp Thr Gly Glu Ser Val Gly Ser Ile
            100                 105                 110

Ser Phe Pro Glu Leu Tyr Gly Arg Lys Glu His Gly Tyr Asn Glu Asn
        115                 120                 125

Tyr Lys Asn Tyr Thr Ala Tyr Met Arg Lys Glu Ala Pro Glu Asp Gly
    130                 135                 140

Gly Gly Lys Asp Ile Glu Ala Ser Phe Asp Asp Glu Ala Val Ile Glu
145                 150                 155                 160

Thr Glu Ala Lys Pro Thr Asp Ile Arg His Val Lys Glu Ile Gly His
                165                 170                 175

Ile Asp Leu Val Ser His Ile Ile Gly Gly Arg Ser Val Asp Gly Arg
            180                 185                 190

Pro Ala Gly Gly Ile Ala Pro Asp Ala Thr Leu His Ile Met Asn Thr
        195                 200                 205

Asn Asp Glu Thr Lys Asn Glu Met Met Val Ala Ala Ile Arg Asn Ala
    210                 215                 220

Trp Val Lys Leu Gly Glu Arg Gly Val Arg Ile Val Asn Asn Ser Phe
225                 230                 235                 240

Gly Thr Thr Ser Arg Ala Gly Thr Ala Asp Leu Phe Gln Ile Ala Asn
                245                 250                 255
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Ser Glu Glu Gln Tyr Arg Gln Ala Leu Leu Asp Tyr Ser Gly Gly Asp
260 265 270

Lys Thr Asp Glu Gly Ile Arg Leu Met Gln Gln Ser Asp Tyr Gly Asn
275 280 285

Leu Ser Tyr His Ile Arg Asn Lys Asn Met Leu Phe Ile Phe Ser Thr
290 295 300

Gly Asn Asp Ala Gln Ala Gln Pro Asn Thr Tyr Ala Leu Leu Pro Phe
305 310 315 320

Tyr Glu Lys Asp Ala Gln Lys Gly Ile Ile Thr Val Ala Gly Val Asp
325 330 335

Arg Ser Gly Glu Lys Phe Lys Arg Glu Met Tyr Gly Glu Pro Gly Thr
340 345 350

Glu Pro Leu Glu Tyr Gly Ser Asn His Cys Gly Ile Thr Ala Met Trp
355 360 365

Cys Leu Ser Ala Pro Tyr Glu Ala Ser Val Arg Phe Thr Arg Thr Asn
370 375 380

Pro Ile Gln Ile Ala Gly Thr Ser Phe Ser Ala Pro Ile Val Thr Gly
385 390 395 400

Thr Ala Ala Leu Leu Leu Gln Lys Tyr Pro Trp Met Ser Asn Asp Asn
405 410 415

Leu Arg Thr Thr Leu Leu Thr Thr Ala Gln Asp Ile Gly Ala Val Gly
420 425 430

Val Asp Ser Lys Phe Gly Trp Gly Leu Leu Asp Ala Gly Lys Ala Met
435 440 445

Asn Gly Pro Ala Ser Phe Pro Phe Gly Asp Phe Thr Ala Asp Thr Lys
450 455 460

Gly Thr Ser Asp Ile Ala Tyr Ser Phe Arg Asn Asp Ile Ser Gly Thr
465 470 475 480

Gly Gly Leu Ile Lys Lys Gly Gly Ser Gln Leu Gln Leu His Gly Asn
485 490 495

Asn Thr Tyr Thr Gly Lys Thr Ile Ile Glu Gly Gly Ser Leu Val Leu
500 505 510

Tyr Gly Asn Asn Lys Ser Asp Met Arg Val Glu Thr Lys Gly Ala Leu
515 520 525

Ile Tyr Asn Gly Ala Ala Ser Gly Gly Ser Leu Asn Ser Asp Gly Ile
530 535 540

Val Tyr Leu Ala Asp Thr Asp Gln Ser Gly Ala Asn Glu Thr Val His
545 550 555 560

Ile Lys Gly Ser Leu Gln Leu Asp Gly Lys Gly Thr Leu Tyr Thr Arg
565 570 575

Leu Gly Lys Leu Leu Lys Val Asp Gly Thr Ala Ile Ile Gly Gly Lys
580 585 590

Leu Tyr Met Ser Ala Arg Gly Lys Gly Ala Gly Tyr Leu Asn Ser Thr
595 600 605

Gly Arg Arg Val Pro Phe Leu Ser Ala Ala Lys Ile Gly Gln Asp Tyr
610 615 620

Ser Phe Phe Thr Asn Ile Glu Thr Asp Gly Gly Leu Leu Ala Ser Leu
625 630 635 640

Asp Ser Val Glu Lys Thr Ala Gly Ser Glu Gly Asp Thr Leu Ser Tyr
645 650 655

Tyr Val Arg Arg Gly Asn Ala Ala Arg Thr Ala Ser Ala Ala Ala His
660 665 670

Ser Ala Pro Ala Gly Leu Lys His Ala Val Glu Gln Gly Gly Ser Asn
675 680 685

Leu Glu Asn Leu Met Val Glu Leu Asp Ala Ser Glu Ser Ser Ala Thr
690 695 700

Pro Glu Thr Val Glu Thr Ala Ala Ala Asp Arg Thr Asp Met Pro Gly
705 710 715 720

Ile Arg Pro Tyr Gly Ala Thr Phe Arg Ala Ala Ala Ala Val Gln His
725 730 735

Ala Asn Ala Ala Asp Gly Val Arg Ile Phe Asn Ser Leu Ala Ala Thr
740 745 750

Val Tyr Ala Asp Ser Thr Ala Ala His Ala Asp Met Gln Gly Arg Arg
755 760 765

Leu Lys Ala Val Ser Asp Gly Leu Asp His Asn Gly Thr Gly Leu Arg
770 775 780

Val Ile Ala Gln Thr Gln Gln Asp Gly Gly Thr Trp Glu Gln Gly Gly
785 790 795 800

Val Glu Gly Lys Met Arg Gly Ser Thr Gln Thr Val Gly Ile Ala Ala
805 810 815

Lys Thr Gly Glu Asn Thr Thr Ala Ala Ala Thr Leu Gly Met Gly Arg
820 825 830

Ser Thr Trp Ser Glu Asn Ser Ala Asn Ala Lys Thr Asp Ser Ile Ser
835 840 845

Leu Phe Ala Gly Ile Arg His Asp Ala Gly Asp Ile Gly Tyr Leu Lys
850 855 860

Gly Leu Phe Ser Tyr Gly Arg Tyr Lys Asn Ser Ile Ser Arg Ser Thr
865 870 875 880

Gly Ala Asp Glu His Ala Glu Gly Ser Val Asn Gly Thr Leu Met Gln
885 890 895

Leu Gly Ala Leu Gly Gly Val Asn Val Pro Phe Ala Ala Thr Gly Asp
900 905 910

Leu Thr Val Glu Gly Gly Leu Arg Tyr Asp Leu Leu Lys Gln Asp Ala
915 920 925

Phe Ala Glu Lys Gly Ser Ala Leu Gly Trp Ser Gly Asn Ser Leu Thr
930 935 940

Glu Gly Thr Leu Val Gly Leu Ala Gly Leu Lys Leu Ser Gln Pro Leu
945 950 955 960

Ser Asp Lys Ala Val Leu Phe Ala Thr Ala Gly Val Glu Arg Asp Leu
965 970 975

Asn Gly Arg Asp Tyr Thr Val Thr Gly Gly Phe Thr Gly Ala Thr Ala
980 985 990

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Ala Thr Gly Lys Thr Gly Ala Arg Asn Met Pro His Thr Arg Leu Val
        995                 1000                1005

Ala Gly Leu Gly Ala Asp Val Glu Phe Gly Asn Gly Trp Asn Gly Leu
    1010                1015                1020

Ala Arg Tyr Ser Tyr Ala Gly Ser Lys Gln Tyr Gly Asn His Ser Gly
1025                1030                1035                1040

Arg Val Gly Val Gly Tyr Arg Phe Leu Glu Gly Gly Gly Gly Thr Gly
                1045                1050                1055

Ser Ala Thr Asn Asp Asp Asp Val Lys Lys Ala Ala Thr Val Ala Ile
            1060                1065                1070

Ala Ala Ala Tyr Asn Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala Gly
        1075                1080                1085

Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp
    1090                1095                1100

Ala Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu
1105                1110                1115                1120

Lys Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys Gln
                1125                1130                1135

Asn Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu
            1140                1145                1150

Thr Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala
        1155                1160                1165

Ala Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile
    1170                1175                1180

Thr Thr Phe Ala Glu Glu Thr Lys Thr Asn Ile Val Lys Ile Asp Glu
1185                1190                1195                1200

Lys Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala Phe
                1205                1210                1215

Asn Asp Ile Ala Asp Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp Glu
            1220                1225                1230

Ala Val Lys Thr Ala Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr Lys
        1235                1240                1245

Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu Thr Ala Ala Gly Lys
    1250                1255                1260

Ala Glu Ala Ala Ala Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala Glu
1265                1270                1275                1280

Ala Val Ala Ala Lys Val Thr Asp Ile Lys Ala Asp Ile Ala Thr Asn
                1285                1290                1295

Lys Asp Asn Ile Ala Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr Arg
            1300                1305                1310

Glu Glu Ser Asp Ser Lys Phe Val Arg Ile Asp Gly Leu Asn Ala Thr
        1315                1320                1325

Thr Glu Lys Leu Asp Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile Ala
    1330                1335                1340

Asp His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp Leu
1345                1350                1355                1360
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Arg Lys Glu Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly
1365 1370 1375

Leu Phe Gln Pro Tyr Asn Val Gly Arg Phe Asn Val Thr Ala Ala Val
1380 1385 1390

Gly Gly Tyr Lys Ser Glu Ser Ala Val Ala Ile Gly Thr Gly Phe Arg
1395 1400 1405

Phe Thr Glu Asn Phe Ala Ala Lys Ala Gly Val Ala Val Gly Thr Ser
1410 1415 1420

Ser Gly Ser Ser Ala Ala Tyr His Val Gly Val Asn Tyr Glu Trp Leu
1425 1430 1435 1440

Glu His His His His His His
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<211> 4179
<212> DNA
<213> Artificial Sequence

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cgcaaagaaa cccgccaagg ccttgcagaa caagccgcgc tctccggtct gttccaacct    4140
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<211> 1392
<212> PRT
<213> Artificial Sequence

<220>
<223> deltaG983-961c

<400> 107

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Asn Ser Arg Ala Thr Thr Ala Lys Ser Ala Ala Val Ser Tyr Ala Gly
            20                  25                  30

Ile Lys Asn Glu Met Cys Lys Asp Arg Ser Met Leu Cys Ala Gly Arg
        35                  40                  45

Asp Asp Val Ala Val Thr Asp Arg Asp Ala Lys Ile Asn Ala Pro Pro
    50                  55                  60

Pro Asn Leu His Thr Gly Asp Phe Pro Asn Pro Asn Asp Ala Tyr Lys
65                  70                  75                  80

Asn Leu Ile Asn Leu Lys Pro Ala Ile Glu Ala Gly Tyr Thr Gly Arg
                85                  90                  95

Gly Val Glu Val Gly Ile Val Asp Thr Gly Glu Ser Val Gly Ser Ile
            100                 105                 110

Ser Phe Pro Glu Leu Tyr Gly Arg Lys Glu His Gly Tyr Asn Glu Asn
        115                 120                 125

Tyr Lys Asn Tyr Thr Ala Tyr Met Arg Lys Glu Ala Pro Glu Asp Gly
    130                 135                 140

Gly Gly Lys Asp Ile Glu Ala Ser Phe Asp Asp Glu Ala Val Ile Glu
145                 150                 155                 160

Thr Glu Ala Lys Pro Thr Asp Ile Arg His Val Lys Glu Ile Gly His
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165 170 175

Ile Asp Leu Val Ser His Ile Ile Gly Gly Arg Ser Val Asp Gly Arg
180 185 190

Pro Ala Gly Gly Ile Ala Pro Asp Ala Thr Leu His Ile Met Asn Thr
195 200 205

Asn Asp Glu Thr Lys Asn Glu Met Met Val Ala Ala Ile Arg Asn Ala
210 215 220

Trp Val Lys Leu Gly Glu Arg Gly Val Arg Ile Val Asn Asn Ser Phe
225 230 235 240

Gly Thr Thr Ser Arg Ala Gly Thr Ala Asp Leu Phe Gln Ile Ala Asn
245 250 255

Ser Glu Glu Gln Tyr Arg Gln Ala Leu Leu Asp Tyr Ser Gly Gly Asp
260 265 270

Lys Thr Asp Glu Gly Ile Arg Leu Met Gln Gln Ser Asp Tyr Gly Asn
275 280 285

Leu Ser Tyr His Ile Arg Asn Lys Asn Met Leu Phe Ile Phe Ser Thr
290 295 300

Gly Asn Asp Ala Gln Ala Gln Pro Asn Thr Tyr Ala Leu Leu Pro Phe
305 310 315 320

Tyr Glu Lys Asp Ala Gln Lys Gly Ile Ile Thr Val Ala Gly Val Asp
325 330 335

Arg Ser Gly Glu Lys Phe Lys Arg Glu Met Tyr Gly Glu Pro Gly Thr
340 345 350

Glu Pro Leu Glu Tyr Gly Ser Asn His Cys Gly Ile Thr Ala Met Trp
355 360 365

Cys Leu Ser Ala Pro Tyr Glu Ala Ser Val Arg Phe Thr Arg Thr Asn
370 375 380

Pro Ile Gln Ile Ala Gly Thr Ser Phe Ser Ala Pro Ile Val Thr Gly
385 390 395 400

Thr Ala Ala Leu Leu Leu Gln Lys Tyr Pro Trp Met Ser Asn Asp Asn
405 410 415

Leu Arg Thr Thr Leu Leu Thr Thr Ala Gln Asp Ile Gly Ala Val Gly
420 425 430

Val Asp Ser Lys Phe Gly Trp Gly Leu Leu Asp Ala Gly Lys Ala Met
435 440 445

Asn Gly Pro Ala Ser Phe Pro Phe Gly Asp Phe Thr Ala Asp Thr Lys
450 455 460

Gly Thr Ser Asp Ile Ala Tyr Ser Phe Arg Asn Asp Ile Ser Gly Thr
465 470 475 480

Gly Gly Leu Ile Lys Lys Gly Gly Ser Gln Leu Gln Leu His Gly Asn
485 490 495

Asn Thr Tyr Thr Gly Lys Thr Ile Ile Glu Gly Gly Ser Leu Val Leu
500 505 510

Tyr Gly Asn Asn Lys Ser Asp Met Arg Val Glu Thr Lys Gly Ala Leu
515 520 525

Ile Tyr Asn Gly Ala Ala Ser Gly Gly Ser Leu Asn Ser Asp Gly Ile

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    530                 535                 540

Val Tyr Leu Ala Asp Thr Asp Gln Ser Gly Ala Asn Glu Thr Val His
545                 550                 555                 560

Ile Lys Gly Ser Leu Gln Leu Asp Gly Lys Gly Thr Leu Tyr Thr Arg
                565                 570                 575

Leu Gly Lys Leu Leu Lys Val Asp Gly Thr Ala Ile Ile Gly Gly Lys
            580                 585                 590

Leu Tyr Met Ser Ala Arg Gly Lys Gly Ala Gly Tyr Leu Asn Ser Thr
        595                 600                 605

Gly Arg Arg Val Pro Phe Leu Ser Ala Ala Lys Ile Gly Gln Asp Tyr
    610                 615                 620

Ser Phe Phe Thr Asn Ile Glu Thr Asp Gly Gly Leu Leu Ala Ser Leu
625                 630                 635                 640

Asp Ser Val Glu Lys Thr Ala Gly Ser Glu Gly Asp Thr Leu Ser Tyr
                645                 650                 655

Tyr Val Arg Arg Gly Asn Ala Ala Arg Thr Ala Ser Ala Ala Ala His
            660                 665                 670

Ser Ala Pro Ala Gly Leu Lys His Ala Val Glu Gln Gly Gly Ser Asn
        675                 680                 685

Leu Glu Asn Leu Met Val Glu Leu Asp Ala Ser Glu Ser Ser Ala Thr
    690                 695                 700

Pro Glu Thr Val Glu Thr Ala Ala Ala Asp Arg Thr Asp Met Pro Gly
705                 710                 715                 720

Ile Arg Pro Tyr Gly Ala Thr Phe Arg Ala Ala Ala Ala Val Gln His
                725                 730                 735

Ala Asn Ala Ala Asp Gly Val Arg Ile Phe Asn Ser Leu Ala Ala Thr
            740                 745                 750

Val Tyr Ala Asp Ser Thr Ala Ala His Ala Asp Met Gln Gly Arg Arg
        755                 760                 765

Leu Lys Ala Val Ser Asp Gly Leu Asp His Asn Gly Thr Gly Leu Arg
    770                 775                 780

Val Ile Ala Gln Thr Gln Gln Asp Gly Gly Thr Trp Glu Gln Gly Gly
785                 790                 795                 800

Val Glu Gly Lys Met Arg Gly Ser Thr Gln Thr Val Gly Ile Ala Ala
                805                 810                 815

Lys Thr Gly Glu Asn Thr Thr Ala Ala Ala Thr Leu Gly Met Gly Arg
            820                 825                 830

Ser Thr Trp Ser Glu Asn Ser Ala Asn Ala Lys Thr Asp Ser Ile Ser
        835                 840                 845

Leu Phe Ala Gly Ile Arg His Asp Ala Gly Asp Ile Gly Tyr Leu Lys
    850                 855                 860

Gly Leu Phe Ser Tyr Gly Arg Tyr Lys Asn Ser Ile Ser Arg Ser Thr
865                 870                 875                 880

Gly Ala Asp Glu His Ala Glu Gly Ser Val Asn Gly Thr Leu Met Gln
                885                 890                 895

Leu Gly Ala Leu Gly Gly Val Asn Val Pro Phe Ala Ala Thr Gly Asp
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900 905 910

Leu Thr Val Glu Gly Gly Leu Arg Tyr Asp Leu Leu Lys Gln Asp Ala
915 920 925

Phe Ala Glu Lys Gly Ser Ala Leu Gly Trp Ser Gly Asn Ser Leu Thr
930 935 940

Glu Gly Thr Leu Val Gly Leu Ala Gly Leu Lys Leu Ser Gln Pro Leu
945 950 955 960

Ser Asp Lys Ala Val Leu Phe Ala Thr Ala Gly Val Glu Arg Asp Leu
965 970 975

Asn Gly Arg Asp Tyr Thr Val Thr Gly Gly Phe Thr Gly Ala Thr Ala
980 985 990

Ala Thr Gly Lys Thr Gly Ala Arg Asn Met Pro His Thr Arg Leu Val
995 1000 1005

Ala Gly Leu Gly Ala Asp Val Glu Phe Gly Asn Gly Trp Asn Gly Leu
1010 1015 1020

Ala Arg Tyr Ser Tyr Ala Gly Ser Lys Gln Tyr Gly Asn His Ser Gly
1025 1030 1035 1040

Arg Val Gly Val Gly Tyr Arg Phe Leu Glu Gly Gly Gly Gly Thr Gly
1045 1050 1055

Ser Ala Thr Asn Asp Asp Asp Val Lys Lys Ala Ala Thr Val Ala Ile
1060 1065 1070

Ala Ala Ala Tyr Asn Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala Gly
1075 1080 1085

Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp
1090 1095 1100

Ala Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu
1105 1110 1115 1120

Lys Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys Gln
1125 1130 1135

Asn Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu
1140 1145 1150

Thr Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala
1155 1160 1165

Ala Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile
1170 1175 1180

Thr Thr Phe Ala Glu Glu Thr Lys Thr Asn Ile Val Lys Ile Asp Glu
1185 1190 1195 1200

Lys Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala Phe
1205 1210 1215

Asn Asp Ile Ala Asp Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp Glu
1220 1225 1230

Ala Val Lys Thr Ala Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr Lys
1235 1240 1245

Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu Thr Ala Ala Gly Lys
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Ala Glu Ala Ala Ala Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala Glu

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Ala Val Ala Ala Lys Val Thr Asp Ile Lys Ala Asp Ile Ala Thr Asn
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Lys Asp Asn Ile Ala Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr Arg
            1300                1305                1310

Glu Glu Ser Asp Ser Lys Phe Val Arg Ile Asp Gly Leu Asn Ala Thr
        1315                1320                1325

Thr Glu Lys Leu Asp Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile Ala
    1330                1335                1340

Asp His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp Leu
1345                1350                1355                1360

Arg Lys Glu Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly
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Leu Phe Gln Pro Tyr Asn Val Gly Leu Glu His His His His His His
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<212> PRT
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Ser Val Arg Lys Asn Glu Lys Leu Lys Leu Ala Ala Gln Gly Ala Glu
        35                  40                  45

Lys Thr Tyr Gly Asn Gly Asp Ser Leu Asn Thr Gly Lys Leu Lys Asn
    50                  55                  60

Asp Lys Val Ser Arg Phe Asp Phe Ile Arg Gln Ile Glu Val Asp Gly
65                  70                  75                  80

Gln Leu Ile Thr Leu Glu Ser Gly Glu Phe Gln Val Tyr Lys Gln Ser
                85                  90                  95

His Ser Ala Leu Thr Ala Phe Gln Thr Glu Gln Ile Gln Asp Ser Glu
            100                 105                 110

His Ser Gly Lys Met Val Ala Lys Arg Gln Phe Arg Ile Gly Asp Ile
        115                 120                 125

Ala Gly Glu His Thr Ser Phe Asp Lys Leu Pro Glu Gly Gly Arg Ala
    130                 135                 140

Thr Tyr Arg Gly Thr Ala Phe Gly Ser Asp Asp Ala Gly Gly Lys Leu
145                 150                 155                 160

Thr Tyr Thr Ile Asp Phe Ala Ala Lys Gln Gly Asn Gly Lys Ile Glu
                165                 170                 175

His Leu Lys Ser Pro Glu Leu Asn Val Asp Leu Ala Ala Ala Asp Ile
            180                 185                 190

Lys Pro Asp Gly Lys Arg His Ala Val Ile Ser Gly Ser Val Leu Tyr
        195                 200                 205

Asn Gln Ala Glu Lys Gly Ser Tyr Ser Leu Gly Ile Phe Gly Gly Lys
    210                 215                 220

Ala Gln Glu Val Ala Gly Ser Ala Glu Val Lys Thr Val Asn Gly Ile
225                 230                 235                 240

Arg His Ile Gly Leu Ala Ala Lys Gln Leu Glu Gly Gly Gly Gly Thr
                245                 250                 255

Gly Ser Ala Thr Asn Asp Asp Asp Val Lys Lys Ala Ala Thr Val Ala
            260                 265                 270

Ile Ala Ala Ala Tyr Asn Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala
        275                 280                 285

Gly Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys
    290                 295                 300

Asp Ala Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly
305                 310                 315                 320

Leu Lys Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys
                325                 330                 335
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Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys
            340                 345                 350

Leu Thr Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp
        355                 360                 365

Ala Ala Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn
    370                 375                 380

Ile Thr Thr Phe Ala Glu Glu Thr Lys Thr Asn Ile Val Lys Ile Asp
385                 390                 395                 400

Glu Lys Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala
                405                 410                 415

Phe Asn Asp Ile Ala Asp Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp
            420                 425                 430

Glu Ala Val Lys Thr Ala Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr
        435                 440                 445

Lys Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu Thr Ala Ala Gly
    450                 455                 460

Lys Ala Glu Ala Ala Ala Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala
465                 470                 475                 480

Glu Ala Val Ala Ala Lys Val Thr Asp Ile Lys Ala Asp Ile Ala Thr
                485                 490                 495

Asn Lys Asp Asn Ile Ala Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr
            500                 505                 510

Arg Glu Glu Ser Asp Ser Lys Phe Val Arg Ile Asp Gly Leu Asn Ala
        515                 520                 525

Thr Thr Glu Lys Leu Asp Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile
    530                 535                 540

Ala Asp His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp
545                 550                 555                 560

Leu Arg Lys Glu Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser
                565                 570                 575

Gly Leu Phe Gln Pro Tyr Asn Val Gly Arg Phe Asn Val Thr Ala Ala
            580                 585                 590

Val Gly Gly Tyr Lys Ser Glu Ser Ala Val Ala Ile Gly Thr Gly Phe
        595                 600                 605

Arg Phe Thr Glu Asn Phe Ala Ala Lys Ala Gly Val Ala Val Gly Thr
    610                 615                 620

Ser Ser Gly Ser Ser Ala Ala Tyr His Val Gly Val Asn Tyr Glu Trp
625                 630                 635                 640

Leu Glu His His His His His His
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ccagaactca atgtcgacct ggccgccgcc gatatcaagc cggatggaaa acgccatgcc 600
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20 25 30

Ser Val Arg Lys Asn Glu Lys Leu Lys Leu Ala Ala Gln Gly Ala Glu
35 40 45

Lys Thr Tyr Gly Asn Gly Asp Ser Leu Asn Thr Gly Lys Leu Lys Asn
50 55 60

Asp Lys Val Ser Arg Phe Asp Phe Ile Arg Gln Ile Glu Val Asp Gly
65 70 75 80

Gln Leu Ile Thr Leu Glu Ser Gly Glu Phe Gln Val Tyr Lys Gln Ser
85 90 95

His Ser Ala Leu Thr Ala Phe Gln Thr Glu Gln Ile Gln Asp Ser Glu
100 105 110

His Ser Gly Lys Met Val Ala Lys Arg Gln Phe Arg Ile Gly Asp Ile
115 120 125

Ala Gly Glu His Thr Ser Phe Asp Lys Leu Pro Glu Gly Gly Arg Ala
130 135 140

Thr Tyr Arg Gly Thr Ala Phe Gly Ser Asp Asp Ala Gly Gly Lys Leu

145 150 155 160

Thr Tyr Thr Ile Asp Phe Ala Ala Lys Gln Gly Asn Gly Lys Ile Glu
165 170 175

His Leu Lys Ser Pro Glu Leu Asn Val Asp Leu Ala Ala Ala Asp Ile
180 185 190

Lys Pro Asp Gly Lys Arg His Ala Val Ile Ser Gly Ser Val Leu Tyr
195 200 205

Asn Gln Ala Glu Lys Gly Ser Tyr Ser Leu Gly Ile Phe Gly Gly Lys
210 215 220

Ala Gln Glu Val Ala Gly Ser Ala Glu Val Lys Thr Val Asn Gly Ile
225 230 235 240

Arg His Ile Gly Leu Ala Ala Lys Gln Leu Glu Gly Gly Gly Gly Thr
245 250 255

Gly Ser Ala Thr Asn Asp Asp Asp Val Lys Lys Ala Ala Thr Val Ala
260 265 270

Ile Ala Ala Ala Tyr Asn Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala
275 280 285

Gly Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys
290 295 300

Asp Ala Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly
305 310 315 320

Leu Lys Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys
325 330 335

Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys
340 345 350

Leu Thr Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp
355 360 365

Ala Ala Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn
370 375 380

Ile Thr Thr Phe Ala Glu Glu Thr Lys Thr Asn Ile Val Lys Ile Asp
385 390 395 400

Glu Lys Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala
405 410 415

Phe Asn Asp Ile Ala Asp Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp
420 425 430

Glu Ala Val Lys Thr Ala Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr
435 440 445

Lys Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu Thr Ala Ala Gly
450 455 460

Lys Ala Glu Ala Ala Ala Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala
465 470 475 480

Glu Ala Val Ala Ala Lys Val Thr Asp Ile Lys Ala Asp Ile Ala Thr
485 490 495

Asn Lys Asp Asn Ile Ala Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr
500 505 510

Arg Glu Glu Ser Asp Ser Lys Phe Val Arg Ile Asp Gly Leu Asn Ala

515 520 525

Thr Thr Glu Lys Leu Asp Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile
530 535 540

Ala Asp His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp
545 550 555 560

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Gly Leu Phe Gln Pro Tyr Asn Val Gly Leu Glu His His His His His
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His

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<400> 113

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            20                  25                  30

Ser Val Arg Lys Asn Glu Lys Leu Lys Leu Ala Ala Gln Gly Ala Glu
        35                  40                  45

Lys Thr Tyr Gly Asn Gly Asp Ser Leu Asn Thr Gly Lys Leu Lys Asn
    50                  55                  60

Asp Lys Val Ser Arg Phe Asp Phe Ile Arg Gln Ile Glu Val Asp Gly
65                  70                  75                  80

Gln Leu Ile Thr Leu Glu Ser Gly Glu Phe Gln Val Tyr Lys Gln Ser
                85                  90                  95

His Ser Ala Leu Thr Ala Phe Gln Thr Glu Gln Ile Gln Asp Ser Glu
            100                 105                 110

His Ser Gly Lys Met Val Ala Lys Arg Gln Phe Arg Ile Gly Asp Ile
        115                 120                 125

Ala Gly Glu His Thr Ser Phe Asp Lys Leu Pro Glu Gly Gly Arg Ala
    130                 135                 140

Thr Tyr Arg Gly Thr Ala Phe Gly Ser Asp Asp Ala Gly Gly Lys Leu
145                 150                 155                 160

Thr Tyr Thr Ile Asp Phe Ala Ala Lys Gln Gly Asn Gly Lys Ile Glu
                165                 170                 175

His Leu Lys Ser Pro Glu Leu Asn Val Asp Leu Ala Ala Ala Asp Ile
            180                 185                 190
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Lys Pro Asp Gly Lys Arg His Ala Val Ile Ser Gly Ser Val Leu Tyr
        195                 200                 205

Asn Gln Ala Glu Lys Gly Ser Tyr Ser Leu Gly Ile Phe Gly Gly Lys
    210                 215                 220

Ala Gln Glu Val Ala Gly Ser Ala Glu Val Lys Thr Val Asn Gly Ile
225                 230                 235                 240

Arg His Ile Gly Leu Ala Ala Lys Gln Leu Glu Gly Ser Gly Gly Gly
                245                 250                 255

Gly Thr Ser Ala Pro Asp Phe Asn Ala Gly Gly Thr Gly Ile Gly Ser
            260                 265                 270

Asn Ser Arg Ala Thr Thr Ala Lys Ser Ala Ala Val Ser Tyr Ala Gly
        275                 280                 285

Ile Lys Asn Glu Met Cys Lys Asp Arg Ser Met Leu Cys Ala Gly Arg
    290                 295                 300

Asp Asp Val Ala Val Thr Asp Arg Asp Ala Lys Ile Asn Ala Pro Pro
305                 310                 315                 320

Pro Asn Leu His Thr Gly Asp Phe Pro Asn Pro Asn Asp Ala Tyr Lys
                325                 330                 335

Asn Leu Ile Asn Leu Lys Pro Ala Ile Glu Ala Gly Tyr Thr Gly Arg
            340                 345                 350

Gly Val Glu Val Gly Ile Val Asp Thr Gly Glu Ser Val Gly Ser Ile
        355                 360                 365

Ser Phe Pro Glu Leu Tyr Gly Arg Lys Glu His Gly Tyr Asn Glu Asn
    370                 375                 380

Tyr Lys Asn Tyr Thr Ala Tyr Met Arg Lys Glu Ala Pro Glu Asp Gly
385                 390                 395                 400

Gly Gly Lys Asp Ile Glu Ala Ser Phe Asp Asp Glu Ala Val Ile Glu
                405                 410                 415

Thr Glu Ala Lys Pro Thr Asp Ile Arg His Val Lys Glu Ile Gly His
            420                 425                 430

Ile Asp Leu Val Ser His Ile Ile Gly Gly Arg Ser Val Asp Gly Arg
        435                 440                 445

Pro Ala Gly Gly Ile Ala Pro Asp Ala Thr Leu His Ile Met Asn Thr
    450                 455                 460

Asn Asp Glu Thr Lys Asn Glu Met Met Val Ala Ala Ile Arg Asn Ala
465                 470                 475                 480

Trp Val Lys Leu Gly Glu Arg Gly Val Arg Ile Val Asn Asn Ser Phe
                485                 490                 495

Gly Thr Thr Ser Arg Ala Gly Thr Ala Asp Leu Phe Gln Ile Ala Asn
            500                 505                 510

Ser Glu Glu Gln Tyr Arg Gln Ala Leu Leu Asp Tyr Ser Gly Gly Asp
        515                 520                 525

Lys Thr Asp Glu Gly Ile Arg Leu Met Gln Gln Ser Asp Tyr Gly Asn
    530                 535                 540

Leu Ser Tyr His Ile Arg Asn Lys Asn Met Leu Phe Ile Phe Ser Thr
545                 550                 555                 560
```

Gly Asn Asp Ala Gln Ala Gln Pro Asn Thr Tyr Ala Leu Leu Pro Phe
565 570 575

Tyr Glu Lys Asp Ala Gln Lys Gly Ile Ile Thr Val Ala Gly Val Asp
580 585 590

Arg Ser Gly Glu Lys Phe Lys Arg Glu Met Tyr Gly Glu Pro Gly Thr
595 600 605

Glu Pro Leu Glu Tyr Gly Ser Asn His Cys Gly Ile Thr Ala Met Trp
610 615 620

Cys Leu Ser Ala Pro Tyr Glu Ala Ser Val Arg Phe Thr Arg Thr Asn
625 630 635 640

Pro Ile Gln Ile Ala Gly Thr Ser Phe Ser Ala Pro Ile Val Thr Gly
645 650 655

Thr Ala Ala Leu Leu Leu Gln Lys Tyr Pro Trp Met Ser Asn Asp Asn
660 665 670

Leu Arg Thr Thr Leu Leu Thr Thr Ala Gln Asp Ile Gly Ala Val Gly
675 680 685

Val Asp Ser Lys Phe Gly Trp Gly Leu Leu Asp Ala Gly Lys Ala Met
690 695 700

Asn Gly Pro Ala Ser Phe Pro Phe Gly Asp Phe Thr Ala Asp Thr Lys
705 710 715 720

Gly Thr Ser Asp Ile Ala Tyr Ser Phe Arg Asn Asp Ile Ser Gly Thr
725 730 735

Gly Gly Leu Ile Lys Lys Gly Gly Ser Gln Leu Gln Leu His Gly Asn
740 745 750

Asn Thr Tyr Thr Gly Lys Thr Ile Ile Glu Gly Gly Ser Leu Val Leu
755 760 765

Tyr Gly Asn Asn Lys Ser Asp Met Arg Val Glu Thr Lys Gly Ala Leu
770 775 780

Ile Tyr Asn Gly Ala Ala Ser Gly Gly Ser Leu Asn Ser Asp Gly Ile
785 790 795 800

Val Tyr Leu Ala Asp Thr Asp Gln Ser Gly Ala Asn Glu Thr Val His
805 810 815

Ile Lys Gly Ser Leu Gln Leu Asp Gly Lys Gly Thr Leu Tyr Thr Arg
820 825 830

Leu Gly Lys Leu Leu Lys Val Asp Gly Thr Ala Ile Ile Gly Gly Lys
835 840 845

Leu Tyr Met Ser Ala Arg Gly Lys Gly Ala Gly Tyr Leu Asn Ser Thr
850 855 860

Gly Arg Arg Val Pro Phe Leu Ser Ala Ala Lys Ile Gly Gln Asp Tyr
865 870 875 880

Ser Phe Phe Thr Asn Ile Glu Thr Asp Gly Gly Leu Leu Ala Ser Leu
885 890 895

Asp Ser Val Glu Lys Thr Ala Gly Ser Glu Gly Asp Thr Leu Ser Tyr
900 905 910

Tyr Val Arg Arg Gly Asn Ala Ala Arg Thr Ala Ser Ala Ala Ala His
915 920 925

```
Ser Ala Pro Ala Gly Leu Lys His Ala Val Glu Gln Gly Gly Ser Asn
    930                 935                 940

Leu Glu Asn Leu Met Val Glu Leu Asp Ala Ser Glu Ser Ser Ala Thr
945                 950                 955                 960

Pro Glu Thr Val Glu Thr Ala Ala Ala Asp Arg Thr Asp Met Pro Gly
                965                 970                 975

Ile Arg Pro Tyr Gly Ala Thr Phe Arg Ala Ala Ala Ala Val Gln His
            980                 985                 990

Ala Asn Ala Ala Asp Gly Val Arg Ile Phe Asn Ser Leu Ala Ala Thr
        995                 1000                1005

Val Tyr Ala Asp Ser Thr Ala Ala His Ala Asp Met Gln Gly Arg Arg
    1010                1015                1020

Leu Lys Ala Val Ser Asp Gly Leu Asp His Asn Gly Thr Gly Leu Arg
1025                1030                1035                1040

Val Ile Ala Gln Thr Gln Gln Asp Gly Gly Thr Trp Glu Gln Gly Gly
                1045                1050                1055

Val Glu Gly Lys Met Arg Gly Ser Thr Gln Thr Val Gly Ile Ala Ala
            1060                1065                1070

Lys Thr Gly Glu Asn Thr Thr Ala Ala Ala Thr Leu Gly Met Gly Arg
        1075                1080                1085

Ser Thr Trp Ser Glu Asn Ser Ala Asn Ala Lys Thr Asp Ser Ile Ser
    1090                1095                1100

Leu Phe Ala Gly Ile Arg His Asp Ala Gly Asp Ile Gly Tyr Leu Lys
1105                1110                1115                1120

Gly Leu Phe Ser Tyr Gly Arg Tyr Lys Asn Ser Ile Ser Arg Ser Thr
                1125                1130                1135

Gly Ala Asp Glu His Ala Glu Gly Ser Val Asn Gly Thr Leu Met Gln
            1140                1145                1150

Leu Gly Ala Leu Gly Gly Val Asn Val Pro Phe Ala Ala Thr Gly Asp
        1155                1160                1165

Leu Thr Val Glu Gly Gly Leu Arg Tyr Asp Leu Leu Lys Gln Asp Ala
    1170                1175                1180

Phe Ala Glu Lys Gly Ser Ala Leu Gly Trp Ser Gly Asn Ser Leu Thr
1185                1190                1195                1200

Glu Gly Thr Leu Val Gly Leu Ala Gly Leu Lys Leu Ser Gln Pro Leu
                1205                1210                1215

Ser Asp Lys Ala Val Leu Phe Ala Thr Ala Gly Val Glu Arg Asp Leu
            1220                1225                1230

Asn Gly Arg Asp Tyr Thr Val Thr Gly Gly Phe Thr Gly Ala Thr Ala
        1235                1240                1245

Ala Thr Gly Lys Thr Gly Ala Arg Asn Met Pro His Thr Arg Leu Val
    1250                1255                1260

Ala Gly Leu Gly Ala Asp Val Glu Phe Gly Asn Gly Trp Asn Gly Leu
1265                1270                1275                1280

Ala Arg Tyr Ser Tyr Ala Gly Ser Lys Gln Tyr Gly Asn His Ser Gly
                1285                1290                1295
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Arg Val Gly Val Gly Tyr Arg Phe Leu Glu His His His His His His
            1300                1305                1310
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<210> 114
<211> 2028
<212> DNA
<213> Artificial Sequence

<220>
<223> deltaG741-ORF46.1

<400> 114

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aaagacaaag gtttgcagtc tttgacgctg gatcagtccg tcaggaaaaa cgagaaactg    120
aagctggcgg cacaaggtgc ggaaaaaact tatggaaacg gtgacagcct caatacgggc    180
aaattgaaga acgacaaggt cagccgtttc gactttatcc gccaaatcga agtggacggg    240
cagctcatta ccttggagag tggagagttc caagtataca aacaaagcca ttccgcctta    300
accgcctttc agaccgagca aatacaagat tcggagcatt ccgggaagat ggttgcgaaa    360
cgccagttca gaatcggcga catagcgggc gaacatacat cttttgacaa gcttcccgaa    420
ggcggcaggg cgacatatcg cgggacggcg ttcggttcag acgatgccgg cggaaaactg    480
acctacacca tagatttcgc cgccaagcag ggaaacggca aaatcgaaca tttgaaatcg    540
ccagaactca atgtcgacct ggccgccgcc gatatcaagc cggatggaaa acgccatgcc    600
gtcatcagcg gttccgtcct ttacaaccaa gccgagaaag gcagttactc cctcggtatc    660
tttggcggaa aagcccagga agttgccggc agcgcggaag tgaaaaccgt aaacggcata    720
cgccatatcg gccttgccgc caagcaactc gacggtggcg gaggcactgg atcctcagat    780
ttggcaaacg attcttttat ccggcaggtt ctcgaccgtc agcatttcga acccgacggg    840
aaataccacc tattcggcag caggggggaa cttgccgagc gcagcggcca tatcggattg    900
ggaaaaatac aaagccatca gttgggcaac ctgatgattc aacaggcggc cattaaagga    960
aatatcggct acattgtccg cttttccgat cacgggcacg aagtccattc ccccttcgac   1020
aaccatgcct cacattccga ttctgatgaa gccggtagtc ccgttgacgg atttagcctt   1080
taccgcatcc attgggacgg atacgaacac catcccgccg acggctatga cgggccacag   1140
ggcggcggct atcccgctcc caaaggcgcg agggatatat acagctacga cataaaaggc   1200
gttgcccaaa atatccgcct caacctgacc gacaaccgca gcaccggaca acggcttgcc   1260
gaccgtttcc acaatgccgg tagtatgctg acgcaaggag taggcgacgg attcaaacgc   1320
gccacccgat acagccccga gctggacaga tcgggcaatg ccgccgaagc cttcaacggc   1380
actgcagata tcgttaaaaa catcatcggc gcggcaggag aaattgtcgg cgcaggcgat   1440
gccgtgcagg gcataagcga aggctcaaac attgctgtca tgcacggctt gggtctgctt   1500
tccaccgaaa acaagatggc gcgcatcaac gatttggcag atatggcgca actcaaagac   1560
tatgccgcag cagccatccg cgattgggca gtccaaaacc ccaatgccgc acaaggcata   1620
gaagccgtca gcaatatctt tatggcagcc atccccatca aagggattgg agctgttcgg   1680
ggaaaatacg gcttgggcgg catcacggca catcctatca agcggtcgca gatgggcgcg   1740
atcgcattgc cgaaagggaa atccgccgtc agcgacaatt ttgccgatgc ggcatacgcc   1800
aaatacccgt ccccttacca ttcccgaaat atccgttcaa acttggagca gcgttacggc   1860
aaagaaaaca tcacctcctc aaccgtgccg ccgtcaaacg gcaaaaatgt caaactggca   1920
gaccaacgcc acccgaagac aggcgtaccg tttgacggta aagggtttcc gaattttgag   1980
aagcacgtga aatatgatac gctcgagcac caccaccacc accactga                 2028
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<210> 115
<211> 675
<212> PRT
<213> Artificial Sequence

<220>
<223> deltaG741-ORF46.1

<400> 115

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Met Val Ala Ala Asp Ile Gly Ala Gly Leu Ala Asp Ala Leu Thr Ala
1               5                   10                  15

Pro Leu Asp His Lys Asp Lys Gly Leu Gln Ser Leu Thr Leu Asp Gln
            20                  25                  30

Ser Val Arg Lys Asn Glu Lys Leu Lys Leu Ala Ala Gln Gly Ala Glu
        35                  40                  45

Lys Thr Tyr Gly Asn Gly Asp Ser Leu Asn Thr Gly Lys Leu Lys Asn
    50                  55                  60
```

Asp Lys Val Ser Arg Phe Asp Phe Ile Arg Gln Ile Glu Val Asp Gly
65 70 75 80

Gln Leu Ile Thr Leu Glu Ser Gly Glu Phe Gln Val Tyr Lys Gln Ser
85 90 95

His Ser Ala Leu Thr Ala Phe Gln Thr Glu Gln Ile Gln Asp Ser Glu
100 105 110

His Ser Gly Lys Met Val Ala Lys Arg Gln Phe Arg Ile Gly Asp Ile
115 120 125

Ala Gly Glu His Thr Ser Phe Asp Lys Leu Pro Glu Gly Gly Arg Ala
130 135 140

Thr Tyr Arg Gly Thr Ala Phe Gly Ser Asp Asp Ala Gly Gly Lys Leu
145 150 155 160

Thr Tyr Thr Ile Asp Phe Ala Ala Lys Gln Gly Asn Gly Lys Ile Glu
165 170 175

His Leu Lys Ser Pro Glu Leu Asn Val Asp Leu Ala Ala Ala Asp Ile
180 185 190

Lys Pro Asp Gly Lys Arg His Ala Val Ile Ser Gly Ser Val Leu Tyr
195 200 205

Asn Gln Ala Glu Lys Gly Ser Tyr Ser Leu Gly Ile Phe Gly Gly Lys
210 215 220

Ala Gln Glu Val Ala Gly Ser Ala Glu Val Lys Thr Val Asn Gly Ile
225 230 235 240

Arg His Ile Gly Leu Ala Ala Lys Gln Leu Asp Gly Gly Gly Gly Thr
245 250 255

Gly Ser Ser Asp Leu Ala Asn Asp Ser Phe Ile Arg Gln Val Leu Asp
260 265 270

Arg Gln His Phe Glu Pro Asp Gly Lys Tyr His Leu Phe Gly Ser Arg
275 280 285

Gly Glu Leu Ala Glu Arg Ser Gly His Ile Gly Leu Gly Lys Ile Gln
290 295 300

Ser His Gln Leu Gly Asn Leu Met Ile Gln Gln Ala Ala Ile Lys Gly
305 310 315 320

Asn Ile Gly Tyr Ile Val Arg Phe Ser Asp His Gly His Glu Val His
325 330 335

Ser Pro Phe Asp Asn His Ala Ser His Ser Asp Ser Asp Glu Ala Gly
340 345 350

Ser Pro Val Asp Gly Phe Ser Leu Tyr Arg Ile His Trp Asp Gly Tyr
355 360 365

Glu His His Pro Ala Asp Gly Tyr Asp Gly Pro Gln Gly Gly Gly Tyr
370 375 380

Pro Ala Pro Lys Gly Ala Arg Asp Ile Tyr Ser Tyr Asp Ile Lys Gly
385 390 395 400

Val Ala Gln Asn Ile Arg Leu Asn Leu Thr Asp Asn Arg Ser Thr Gly
405 410 415

Gln Arg Leu Ala Asp Arg Phe His Asn Ala Gly Ser Met Leu Thr Gln
420 425 430

Gly Val Gly Asp Gly Phe Lys Arg Ala Thr Arg Tyr Ser Pro Glu Leu
435 440 445

Asp Arg Ser Gly Asn Ala Ala Glu Ala Phe Asn Gly Thr Ala Asp Ile
450 455 460

Val Lys Asn Ile Ile Gly Ala Ala Gly Glu Ile Val Gly Ala Gly Asp
465 470 475 480

Ala Val Gln Gly Ile Ser Glu Gly Ser Asn Ile Ala Val Met His Gly
485 490 495

Leu Gly Leu Leu Ser Thr Glu Asn Lys Met Ala Arg Ile Asn Asp Leu
500 505 510

Ala Asp Met Ala Gln Leu Lys Asp Tyr Ala Ala Ala Ala Ile Arg Asp
515 520 525

Trp Ala Val Gln Asn Pro Asn Ala Ala Gln Gly Ile Glu Ala Val Ser
530 535 540

Asn Ile Phe Met Ala Ala Ile Pro Ile Lys Gly Ile Gly Ala Val Arg
545 550 555 560

Gly Lys Tyr Gly Leu Gly Gly Ile Thr Ala His Pro Ile Lys Arg Ser
565 570 575

Gln Met Gly Ala Ile Ala Leu Pro Lys Gly Lys Ser Ala Val Ser Asp
580 585 590

Asn Phe Ala Asp Ala Ala Tyr Ala Lys Tyr Pro Ser Pro Tyr His Ser
595 600 605

Arg Asn Ile Arg Ser Asn Leu Glu Gln Arg Tyr Gly Lys Glu Asn Ile
610 615 620

Thr Ser Ser Thr Val Pro Pro Ser Asn Gly Lys Asn Val Lys Leu Ala
625 630 635 640

Asp Gln Arg His Pro Lys Thr Gly Val Pro Phe Asp Gly Lys Gly Phe
645 650 655

Pro Asn Phe Glu Lys His Val Lys Tyr Asp Thr Leu Glu His His His
660 665 670

His His His
675

<210> 116
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<223> Novel protein

<400> 116
Met Lys Lys Tyr Leu Phe Arg Ala Ala Leu Tyr Gly Ile Ala Ala Ala
1 5 10 15

Ile Leu Ala Ala Ala Ile Pro Ala Gly Asn Asp Ala Thr Thr Lys Pro
20 25 30

Asp Leu Tyr Tyr Leu Lys Asn Glu Gln Ala Ile Asp Ser Leu Lys Leu
35 40 45

Leu Pro Pro Pro Pro Glu Val Gly Ser Ile Gln Phe Leu Asn Asp Gln
50 55 60

```
Ala Met Tyr Glu Lys Gly Arg Met Leu Arg Asn Thr Glu Arg Gly Lys
65                  70                  75                  80

Gln Ala Gln Ala Asp Ala Asp Leu Ala Ala Gly Gly Val Ala Thr Ala
                85                  90                  95

Phe Ser Gly Ala Phe Gly Tyr Pro Ile Thr Glu Lys Asp Ser Pro Glu
            100                 105                 110

Leu Tyr Lys Leu Leu Thr Asn Met Ile Glu Asp Ala Gly Asp Leu Ala
        115                 120                 125

Thr Arg Ser Ala Lys Glu His Tyr Met Arg Ile Arg Pro Phe Ala Phe
    130                 135                 140

Tyr Gly Thr Glu Thr Cys Asn Thr Lys Asp Gln Lys Lys Leu Ser Thr
145                 150                 155                 160

Asn Gly Ser Tyr Pro Ser Gly His Thr Ser Ile Gly Trp Ala Thr Ala
                165                 170                 175

Leu Val Leu Ala Glu Val Asn Pro Ala Asn Gln Asp Ala Ile Leu Glu
            180                 185                 190

Arg Gly Tyr Gln Leu Gly Gln Ser Arg Val Ile Cys Gly Tyr His Trp
        195                 200                 205

Gln Ser Asp Val Asp Ala Ala Arg Ile Val Gly Ser Ala Ala Val Ala
    210                 215                 220

Thr Leu His Ser Asp Pro Ala Phe Gln Ala Gln Leu Ala Lys Ala Lys
225                 230                 235                 240

Gln Glu Phe Ala Gln Lys Ser Gln Lys
                245
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<210>   117
<211>   66
<212>   DNA
<213>   Artificial Sequence

<220>
<223>   L1 linker

<220>
<221>   N
<222>   13
<223>   A, T/U, G or C

<400>   117
tatgaartay ytnttymgcg ccgccctgta cggcatcgcc gccgccatcc tcgccgccgc    60
gatccc                                                                66

<210>   118
<211>   69
<212>   DNA
<213>   Artificial Sequence

<220>
<223>   S1 linker

<220>
<221>   N
<222>   25, 28
<223>   A, T/U, G or C

<400>   118
tatgaaaaaa tacctattcc grgcngcnyt rtayggsatc gccgccgcca tcctcgccgc    60
cgcgatccc                                                             69
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<210>  119
<211>  27
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  9L1-a

<400>  119
atgaagaagt accttttcag cgccgcc                                    27

<210>  120
<211>  27
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  9L1-e

<400>  120
atgaaaaaat actttttccg cgccgcc                                    27

<210>  121
<211>  27
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  9L1-d

<400>  121
atgaaaaaat actttttccg cgccgcc                                    27

<210>  122
<211>  60
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  9L1-f

<400>  122
atgaaaaaat atctctttag cgccgccctg tacggcatcg ccgccgccat cctcgccgcc   60

<210>  123
<211>  60
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  919sp

<400>  123
atgaaaaaat acctattccg cgccgccctg tacggcatcg ccgccgccat cctcgccgcc   60

<210>  124
<211>  9
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  9L1a

<400>  124
Met Lys Lys Tyr Leu Phe Ser Ala Ala
1               5

<210>  125
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<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> 9L1e

<400> 125
Met Lys Lys Tyr Phe Phe Arg Ala Ala
1 5

<210> 126
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> 9L1d

<400> 126
Met Lys Lys Tyr Phe Phe Arg Ala Ala
1 5

<210> 127
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> 9L1f

<400> 127
Met Lys Lys Tyr Leu Phe Ser Ala Ala Leu Tyr Gly Ile Ala Ala Ala
1 5 10 15

Ile Leu Ala Ala
20

<210> 128
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> 9L1sp

<400> 128
Met Lys Lys Tyr Leu Phe Arg Ala Ala Leu Tyr Gly Ile Ala Ala Ala
1 5 10 15

Ile Leu Ala Ala
20

<210> 129
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> 9S1-e

<400> 129
atgaaaaaat acctattcat cgccgccgcc atcctcgccg cc 42

<210> 130
<211> 60
<212> DNA
<213> Artificial Sequence

<220>
<223> 9S1-c

<400> 130
atgaaaaaat acctattccg agctgcccaa tacggcatcg ccgccgccat cctcgccgcc 60

<210> 131
<211> 60
<212> DNA
<213> Artificial Sequence

<220>
<223> 9S1-b

<400> 131
atgaaaaaat acctattccg ggccgcccaa tacggcatcg ccgccgccat cctcgccgcc 60

<210> 132
<211> 60
<212> DNA
<213> Artificial Sequence

<220>
<223> 9S1-i

<400> 132
atgaaaaaat acctattccg ggcggctttg tacgggatcg ccgccgccat cctcgccgcc 60

<210> 133
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> 9S1e

<400> 133
Met Lys Lys Tyr Leu Phe Ile Ala Ala Ala Ile Leu Ala Ala
1   5   10

<210> 134
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> 9S1c

<400> 134
Met Lys Lys Tyr Leu Phe Arg Ala Ala Gln Tyr Gly Ile Ala Ala Ala
1   5   10   15

Ile Leu Ala Ala
            20

<210> 135
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> 9S1b

<400> 135
Met Lys Lys Tyr Leu Phe Arg Ala Ala Gln Tyr Gly Ile Ala Ala Ala
1   5   10   15

Ile Leu Ala Ala
            20

<210> 136
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> 9S1i

<400> 136
Met Lys Lys Tyr Leu Phe Arg Ala Ala Leu Tyr Gly Ile Ala Ala Ala
1   5   10   15

Ile Leu Ala Ala
            20

<210> 137
<211> 467
<212> PRT
<213> Artificial Sequence

<220>
<223> 730

<400> 137
Val Lys Pro Leu Arg Arg Leu Thr Asn Leu Leu Ala Ala Cys Ala Val
1   5   10   15

Ala Ala Ala Ala Leu Ile Gln Pro Ala Leu Ala Ala Asp Leu Ala Gln
            20   25   30

Asp Pro Phe Ile Thr Asp Asn Ala Gln Arg Gln His Tyr Glu Pro Gly
        35   40   45

Gly Lys Tyr His Leu Phe Gly Asp Pro Arg Gly Ser Val Ser Asp Arg
    50   55   60

Thr Gly Lys Ile Asn Val Ile Gln Asp Tyr Thr His Gln Met Gly Asn
65   70   75   80

Leu Leu Ile Gln Gln Ala Asn Ile Asn Gly Thr Ile Gly Tyr His Thr
                85   90   95

Arg Phe Ser Gly His Gly His Glu Glu His Ala Pro Phe Asp Asn His
            100   105   110

Ala Ala Asp Ser Ala Ser Glu Glu Lys Gly Asn Val Asp Glu Gly Phe
        115   120   125

Thr Val Tyr Arg Leu Asn Trp Glu Gly His Glu His His Pro Ala Asp
    130   135   140

Ala Tyr Asp Gly Pro Lys Gly Gly Asn Tyr Pro Lys Pro Thr Gly Ala
145   150   155   160

Arg Asp Glu Tyr Thr Tyr His Val Asn Gly Thr Ala Arg Ser Ile Lys
                165   170   175

Leu Asn Pro Thr Asp Thr Arg Ser Ile Arg Gln Arg Ile Ser Asp Asn
            180   185   190

Tyr Ser Asn Leu Gly Ser Asn Phe Ser Asp Arg Ala Asp Glu Ala Asn
        195   200   205

Arg Lys Met Phe Glu His Asn Ala Lys Leu Asp Arg Trp Gly Asn Ser
    210   215   220

Met Glu Phe Ile Asn Gly Val Ala Ala Gly Ala Leu Asn Pro Phe Ile
225   230   235   240

Ser Ala Gly Glu Ala Leu Gly Ile Gly Asp Ile Leu Tyr Gly Thr Arg
245 250 255

Tyr Ala Ile Asp Lys Ala Ala Met Arg Asn Ile Ala Pro Leu Pro Ala
260 265 270

Glu Gly Lys Phe Ala Val Ile Gly Gly Leu Gly Ser Val Ala Gly Phe
275 280 285

Glu Lys Asn Thr Arg Glu Ala Val Asp Arg Trp Ile Gln Glu Asn Pro
290 295 300

Asn Ala Ala Glu Thr Val Glu Ala Val Phe Asn Val Ala Ala Ala Ala
305 310 315 320

Lys Val Ala Lys Leu Ala Lys Ala Ala Lys Pro Gly Lys Ala Ala Val
325 330 335

Ser Gly Asp Phe Ala Asp Ser Tyr Lys Lys Lys Leu Ala Leu Ser Asp
340 345 350

Ser Ala Arg Gln Leu Tyr Gln Asn Ala Lys Tyr Arg Glu Ala Leu Asp
355 360 365

Ile His Tyr Glu Asp Leu Ile Arg Arg Lys Thr Asp Gly Ser Ser Lys
370 375 380

Phe Ile Asn Gly Arg Glu Ile Asp Ala Val Thr Asn Asp Ala Leu Ile
385 390 395 400

Gln Ala Lys Arg Thr Ile Ser Ala Ile Asp Lys Pro Lys Asn Phe Leu
405 410 415

Asn Gln Lys Asn Arg Lys Gln Ile Lys Ala Thr Ile Glu Ala Ala Asn
420 425 430

Gln Gln Gly Lys Arg Ala Glu Phe Trp Phe Lys Tyr Gly Val His Ser
435 440 445

Gln Val Lys Ser Tyr Ile Glu Ser Lys Gly Gly Ile Val Lys Thr Gly
450 455 460

Leu Gly Asp
465

<210> 138
<211> 377
<212> PRT
<213> Artificial Sequence

<220>
<223> 730-C1

<400> 138
Met Ala Asp Leu Ala Gln Asp Pro Phe Ile Thr Asp Asn Ala Gln Arg
1 5 10 15

Gln His Tyr Glu Pro Gly Gly Lys Tyr His Leu Phe Gly Asp Pro Arg
20 25 30

Gly Ser Val Ser Asp Arg Thr Gly Lys Ile Asn Val Ile Gln Asp Tyr
35 40 45

Thr His Gln Met Gly Asn Leu Leu Ile Gln Gln Ala Asn Ile Asn Gly
50 55 60

Thr Ile Gly Tyr His Thr Arg Phe Ser Gly His Gly His Glu Glu His
65 70 75 80

```
Ala Pro Phe Asp Asn His Ala Ala Asp Ser Ala Ser Glu Glu Lys Gly
                85                  90                  95

Asn Val Asp Glu Gly Phe Thr Val Tyr Arg Leu Asn Trp Glu Gly His
            100                 105                 110

Glu His His Pro Ala Asp Ala Tyr Asp Gly Pro Lys Gly Gly Asn Tyr
        115                 120                 125

Pro Lys Pro Thr Gly Ala Arg Asp Glu Tyr Thr Tyr His Val Asn Gly
    130                 135                 140

Thr Ala Arg Ser Ile Lys Leu Asn Pro Thr Asp Thr Arg Ser Ile Arg
145                 150                 155                 160

Gln Arg Ile Ser Asp Asn Tyr Ser Asn Leu Gly Ser Asn Phe Ser Asp
                165                 170                 175

Arg Ala Asp Glu Ala Asn Arg Lys Met Phe Glu His Asn Ala Lys Leu
            180                 185                 190

Asp Arg Trp Gly Asn Ser Met Glu Phe Ile Asn Gly Val Ala Ala Gly
        195                 200                 205

Ala Leu Asn Pro Phe Ile Ser Ala Gly Glu Ala Leu Gly Ile Gly Asp
    210                 215                 220

Ile Leu Tyr Gly Thr Arg Tyr Ala Ile Asp Lys Ala Ala Met Arg Asn
225                 230                 235                 240

Ile Ala Pro Leu Pro Ala Glu Gly Lys Phe Ala Val Ile Gly Gly Leu
                245                 250                 255

Gly Ser Val Ala Gly Phe Glu Lys Asn Thr Arg Glu Ala Val Asp Arg
            260                 265                 270

Trp Ile Gln Glu Asn Pro Asn Ala Ala Glu Thr Val Glu Ala Val Phe
        275                 280                 285

Asn Val Ala Ala Ala Ala Lys Val Ala Lys Leu Ala Lys Ala Ala Lys
    290                 295                 300

Pro Gly Lys Ala Ala Val Ser Gly Asp Phe Ala Asp Ser Tyr Lys Lys
305                 310                 315                 320

Lys Leu Ala Leu Ser Asp Ser Ala Arg Gln Leu Tyr Gln Asn Ala Lys
                325                 330                 335

Tyr Arg Glu Ala Leu Asp Ile His Tyr Glu Asp Leu Ile Arg Arg Lys
            340                 345                 350

Thr Asp Gly Ser Ser Lys Phe Ile Asn Gly Arg Glu Ile Asp Ala Val
        355                 360                 365

Thr Asn Asp Ala Leu Ile Gln Ala Arg
    370                 375

<210>   139
<211>   353
<212>   PRT
<213>   Artificial Sequence

<220>
<223>   730-C2

<400>   139
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Gln His Tyr Glu Pro Gly Gly Lys Tyr His Leu Phe Gly Asp Pro Arg
20 25 30

Gly Ser Val Ser Asp Arg Thr Gly Lys Ile Asn Val Ile Gln Asp Tyr
35 40 45

Thr His Gln Met Gly Asn Leu Leu Ile Gln Gln Ala Asn Ile Asn Gly
50 55 60

Thr Ile Gly Tyr His Thr Arg Phe Ser Gly His Gly His Glu Glu His
65 70 75 80

Ala Pro Phe Asp Asn His Ala Ala Asp Ser Ala Ser Glu Glu Lys Gly
85 90 95

Asn Val Asp Glu Gly Phe Thr Val Tyr Arg Leu Asn Trp Glu Gly His
100 105 110

Glu His His Pro Ala Asp Ala Tyr Asp Gly Pro Lys Gly Gly Asn Tyr
115 120 125

Pro Lys Pro Thr Gly Ala Arg Asp Glu Tyr Thr Tyr His Val Asn Gly
130 135 140

Thr Ala Arg Ser Ile Lys Leu Asn Pro Thr Asp Thr Arg Ser Ile Arg
145 150 155 160

Gln Arg Ile Ser Asp Asn Tyr Ser Asn Leu Gly Ser Asn Phe Ser Asp
165 170 175

Arg Ala Asp Glu Ala Asn Arg Lys Met Phe Glu His Asn Ala Lys Leu
180 185 190

Asp Arg Trp Gly Asn Ser Met Glu Phe Ile Asn Gly Val Ala Ala Gly
195 200 205

Ala Leu Asn Pro Phe Ile Ser Ala Gly Glu Ala Leu Gly Ile Gly Asp
210 215 220

Ile Leu Tyr Gly Thr Arg Tyr Ala Ile Asp Lys Ala Ala Met Arg Asn
225 230 235 240

Ile Ala Pro Leu Pro Ala Glu Gly Lys Phe Ala Val Ile Gly Gly Leu
245 250 255

Gly Ser Val Ala Gly Phe Glu Lys Asn Thr Arg Glu Ala Val Asp Arg
260 265 270

Trp Ile Gln Glu Asn Pro Asn Ala Ala Glu Thr Val Glu Ala Val Phe
275 280 285

Asn Val Ala Ala Ala Ala Lys Val Ala Lys Leu Ala Lys Ala Ala Lys
290 295 300

Pro Gly Lys Ala Ala Val Ser Gly Asp Phe Ala Asp Ser Tyr Lys Lys
305 310 315 320

Lys Leu Ala Leu Ser Asp Ser Ala Arg Gln Leu Tyr Gln Asn Ala Lys
325 330 335

Tyr Arg Glu Ala Leu Gly Lys Val Arg Ile Ser Gly Glu Ile Leu Leu
340 345 350

Gly

<210> 140
<211> 2019

<212> DNA
<213> Artificial Sequence

<220>
<223> ORF46.1-741

<400> 140
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tatcgcggga cggcgttcgg ttcagacgat gccggcggaa aactgaccta caccatagat  1740
ttcgccgcca agcagggaaa cggcaaaatc gaacatttga aatcgccaga actcaatgtc  1800
gacctggccg ccgccgatat caagccggat ggaaaacgcc atgccgtcat cagcggttcc  1860
gtcctttaca accaagccga gaaaggcagt tactccctcg gtatctttgg cggaaaagcc  1920
caggaagttg ccggcagcgc ggaagtgaaa accgtaaacg gcatacgcca tatcggcctt  1980
gccgccaagc aactcgagca ccaccaccac caccactga                          2019
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<210> 141
<211> 672
<212> PRT
<213> Artificial Sequence

<220>
<223> ORF46.1-741

<400> 141
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Gln His Phe Glu Pro Asp Gly Lys Tyr His Leu Phe Gly Ser Arg Gly
            20                  25                  30

Glu Leu Ala Glu Arg Ser Gly His Ile Gly Leu Gly Lys Ile Gln Ser
        35                  40                  45

His Gln Leu Gly Asn Leu Met Ile Gln Gln Ala Ala Ile Lys Gly Asn
    50                  55                  60

Ile Gly Tyr Ile Val Arg Phe Ser Asp His Gly His Glu Val His Ser
65                  70                  75                  80

Pro Phe Asp Asn His Ala Ser His Ser Asp Ser Asp Glu Ala Gly Ser
                85                  90                  95
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Pro Val Asp Gly Phe Ser Leu Tyr Arg Ile His Trp Asp Gly Tyr Glu
100 105 110

His His Pro Ala Asp Gly Tyr Asp Gly Pro Gln Gly Gly Gly Tyr Pro
115 120 125

Ala Pro Lys Gly Ala Arg Asp Ile Tyr Ser Tyr Asp Ile Lys Gly Val
130 135 140

Ala Gln Asn Ile Arg Leu Asn Leu Thr Asp Asn Arg Ser Thr Gly Gln
145 150 155 160

Arg Leu Ala Asp Arg Phe His Asn Ala Gly Ser Met Leu Thr Gln Gly
165 170 175

Val Gly Asp Gly Phe Lys Arg Ala Thr Arg Tyr Ser Pro Glu Leu Asp
180 185 190

Arg Ser Gly Asn Ala Ala Glu Ala Phe Asn Gly Thr Ala Asp Ile Val
195 200 205

Lys Asn Ile Ile Gly Ala Ala Gly Glu Ile Val Gly Ala Gly Asp Ala
210 215 220

Val Gln Gly Ile Ser Glu Gly Ser Asn Ile Ala Val Met His Gly Leu
225 230 235 240

Gly Leu Leu Ser Thr Glu Asn Lys Met Ala Arg Ile Asn Asp Leu Ala
245 250 255

Asp Met Ala Gln Leu Lys Asp Tyr Ala Ala Ala Ala Ile Arg Asp Trp
260 265 270

Ala Val Gln Asn Pro Asn Ala Ala Gln Gly Ile Glu Ala Val Ser Asn
275 280 285

Ile Phe Met Ala Ala Ile Pro Ile Lys Gly Ile Gly Ala Val Arg Gly
290 295 300

Lys Tyr Gly Leu Gly Gly Ile Thr Ala His Pro Ile Lys Arg Ser Gln
305 310 315 320

Met Gly Ala Ile Ala Leu Pro Lys Gly Lys Ser Ala Val Ser Asp Asn
325 330 335

Phe Ala Asp Ala Ala Tyr Ala Lys Tyr Pro Ser Pro Tyr His Ser Arg
340 345 350

Asn Ile Arg Ser Asn Leu Glu Gln Arg Tyr Gly Lys Glu Asn Ile Thr
355 360 365

Ser Ser Thr Val Pro Pro Ser Asn Gly Lys Asn Val Lys Leu Ala Asp
370 375 380

Gln Arg His Pro Lys Thr Gly Val Pro Phe Asp Gly Lys Gly Phe Pro
385 390 395 400

Asn Phe Glu Lys His Val Lys Tyr Asp Thr Gly Ser Gly Gly Gly Gly
405 410 415

Val Ala Ala Asp Ile Gly Ala Gly Leu Ala Asp Ala Leu Thr Ala Pro
420 425 430

Leu Asp His Lys Asp Lys Gly Leu Gln Ser Leu Thr Leu Asp Gln Ser
435 440 445

Val Arg Lys Asn Glu Lys Leu Lys Leu Ala Ala Gln Gly Ala Glu Lys
450 455 460

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Thr Tyr Gly Asn Gly Asp Ser Leu Asn Thr Gly Lys Leu Lys Asn Asp
465                 470                 475                 480

Lys Val Ser Arg Phe Asp Phe Ile Arg Gln Ile Glu Val Asp Gly Gln
                485                 490                 495

Leu Ile Thr Leu Glu Ser Gly Glu Phe Gln Val Tyr Lys Gln Ser His
            500                 505                 510

Ser Ala Leu Thr Ala Phe Gln Thr Glu Gln Ile Gln Asp Ser Glu His
        515                 520                 525

Ser Gly Lys Met Val Ala Lys Arg Gln Phe Arg Ile Gly Asp Ile Ala
    530                 535                 540

Gly Glu His Thr Ser Phe Asp Lys Leu Pro Glu Gly Gly Arg Ala Thr
545                 550                 555                 560

Tyr Arg Gly Thr Ala Phe Gly Ser Asp Asp Ala Gly Gly Lys Leu Thr
                565                 570                 575

Tyr Thr Ile Asp Phe Ala Ala Lys Gln Gly Asn Gly Lys Ile Glu His
            580                 585                 590

Leu Lys Ser Pro Glu Leu Asn Val Asp Leu Ala Ala Ala Asp Ile Lys
        595                 600                 605

Pro Asp Gly Lys Arg His Ala Val Ile Ser Gly Ser Val Leu Tyr Asn
    610                 615                 620

Gln Ala Glu Lys Gly Ser Tyr Ser Leu Gly Ile Phe Gly Gly Lys Ala
625                 630                 635                 640

Gln Glu Val Ala Gly Ser Ala Glu Val Lys Thr Val Asn Gly Ile Arg
                645                 650                 655

His Ile Gly Leu Ala Ala Lys Gln Leu Glu His His His His His His
            660                 665                 670


<210>   142
<211>   2421
<212>   DNA
<213>   Artificial Sequence

<220>
<223>   ORF46.1-961

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attaaaggaa atatcggcta cattgtccgc ttttccgatc acgggcacga agtccattcc    240
cccttcgaca accatgcctc acattccgat tctgatgaag ccggtagtcc cgttgacgga    300
tttagccttt accgcatcca ttgggacgga tacgaacacc atcccgccga cggctatgac    360
gggccacagg gcggcggcta tcccgctccc aaaggcgcga gggatatata cagctacgac    420
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cggcttgccg accgtttcca caatgccggt agtatgctga cgcaaggagt aggcgacgga    540
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gcaggcgatg ccgtgcaggg cataagcgaa ggctcaaaca ttgctgtcat gcacggcttg    720
ggtctgcttt ccaccgaaaa caagatggcg cgcatcaacg atttggcaga tatggcgcaa    780
ctcaaagact atgccgcagc agccatccgc gattgggcag tccaaaaccc caatgccgca    840
caaggcatag aagccgtcag caatatcttt atggcagcca tccccatcaa agggattgga    900
gctgttcggg gaaaatacgg cttgggcggc atcacggcac atcctatcaa gcggtcgcag    960
atgggcgcga tcgcattgcc gaaagggaaa tccgccgtca gcgacaattt tgccgatgcg   1020
gcatacgcca aatacccgtc cccttaccat tcccgaaata tccgttcaaa cttggagcag   1080
cgttacggca aagaaaacat cacctcctca accgtgccgc cgtcaaacgg caaaaatgtc   1140
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cagacggccg aagaaaccaa acaaaacgtc gatgccaaag taaaagctgc agaaactgca   1860
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gccatcggta ccggcttccg ctttaccgaa aactttgccg ccaaagcagg cgtggcagtc   2340
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<210> 143
<211> 806
<212> PRT
<213> Artificial Sequence

<220>
<223> ORF46.1-961

<400> 143

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Gln His Phe Glu Pro Asp Gly Lys Tyr His Leu Phe Gly Ser Arg Gly
            20                  25                  30

Glu Leu Ala Glu Arg Ser Gly His Ile Gly Leu Gly Lys Ile Gln Ser
        35                  40                  45

His Gln Leu Gly Asn Leu Met Ile Gln Gln Ala Ala Ile Lys Gly Asn
    50                  55                  60

Ile Gly Tyr Ile Val Arg Phe Ser Asp His Gly His Glu Val His Ser
65                  70                  75                  80

Pro Phe Asp Asn His Ala Ser His Ser Asp Ser Asp Glu Ala Gly Ser
                85                  90                  95

Pro Val Asp Gly Phe Ser Leu Tyr Arg Ile His Trp Asp Gly Tyr Glu
            100                 105                 110

His His Pro Ala Asp Gly Tyr Asp Gly Pro Gln Gly Gly Gly Tyr Pro
        115                 120                 125

Ala Pro Lys Gly Ala Arg Asp Ile Tyr Ser Tyr Asp Ile Lys Gly Val
    130                 135                 140

Ala Gln Asn Ile Arg Leu Asn Leu Thr Asp Asn Arg Ser Thr Gly Gln
145                 150                 155                 160

Arg Leu Ala Asp Arg Phe His Asn Ala Gly Ser Met Leu Thr Gln Gly
                165                 170                 175

Val Gly Asp Gly Phe Lys Arg Ala Thr Arg Tyr Ser Pro Glu Leu Asp
            180                 185                 190

Arg Ser Gly Asn Ala Ala Glu Ala Phe Asn Gly Thr Ala Asp Ile Val
        195                 200                 205
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Lys Asn Ile Ile Gly Ala Ala Gly Glu Ile Val Gly Ala Gly Asp Ala
    210                 215                 220

Val Gln Gly Ile Ser Glu Gly Ser Asn Ile Ala Val Met His Gly Leu
225                 230                 235                 240

Gly Leu Leu Ser Thr Glu Asn Lys Met Ala Arg Ile Asn Asp Leu Ala
                245                 250                 255

Asp Met Ala Gln Leu Lys Asp Tyr Ala Ala Ala Ala Ile Arg Asp Trp
            260                 265                 270

Ala Val Gln Asn Pro Asn Ala Ala Gln Gly Ile Glu Ala Val Ser Asn
        275                 280                 285

Ile Phe Met Ala Ala Ile Pro Ile Lys Gly Ile Gly Ala Val Arg Gly
    290                 295                 300

Lys Tyr Gly Leu Gly Gly Ile Thr Ala His Pro Ile Lys Arg Ser Gln
305                 310                 315                 320

Met Gly Ala Ile Ala Leu Pro Lys Gly Lys Ser Ala Val Ser Asp Asn
                325                 330                 335

Phe Ala Asp Ala Ala Tyr Ala Lys Tyr Pro Ser Pro Tyr His Ser Arg
            340                 345                 350

Asn Ile Arg Ser Asn Leu Glu Gln Arg Tyr Gly Lys Glu Asn Ile Thr
        355                 360                 365

Ser Ser Thr Val Pro Pro Ser Asn Gly Lys Asn Val Lys Leu Ala Asp
    370                 375                 380

Gln Arg His Pro Lys Thr Gly Val Pro Phe Asp Gly Lys Gly Phe Pro
385                 390                 395                 400

Asn Phe Glu Lys His Val Lys Tyr Asp Thr Gly Ser Gly Gly Gly Gly
                405                 410                 415

Ala Thr Asn Asp Asp Asp Val Lys Lys Ala Ala Thr Val Ala Ile Ala
            420                 425                 430

Ala Ala Tyr Asn Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala Gly Glu
        435                 440                 445

Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp Ala
    450                 455                 460

Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu Lys
465                 470                 475                 480

Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys Gln Asn
                485                 490                 495

Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu Thr
            500                 505                 510

Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala Ala
        515                 520                 525

Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile Thr
    530                 535                 540

Thr Phe Ala Glu Glu Thr Lys Thr Asn Ile Val Lys Ile Asp Glu Lys
545                 550                 555                 560

Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala Phe Asn
                565                 570                 575
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Asp Ile Ala Asp Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp Glu Ala
580 585 590

Val Lys Thr Ala Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr Lys Gln
595 600 605

Asn Val Asp Ala Lys Val Lys Ala Ala Glu Thr Ala Ala Gly Lys Ala
610 615 620

Glu Ala Ala Ala Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala Glu Ala
625 630 635 640

Val Ala Ala Lys Val Thr Asp Ile Lys Ala Asp Ile Ala Thr Asn Lys
645 650 655

Asp Asn Ile Ala Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr Arg Glu
660 665 670

Glu Ser Asp Ser Lys Phe Val Arg Ile Asp Gly Leu Asn Ala Thr Thr
675 680 685

Glu Lys Leu Asp Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile Ala Asp
690 695 700

His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp Leu Arg
705 710 715 720

Lys Glu Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly Leu
725 730 735

Phe Gln Pro Tyr Asn Val Gly Arg Phe Asn Val Thr Ala Ala Val Gly
740 745 750

Gly Tyr Lys Ser Glu Ser Ala Val Ala Ile Gly Thr Gly Phe Arg Phe
755 760 765

Thr Glu Asn Phe Ala Ala Lys Ala Gly Val Ala Val Gly Thr Ser Ser
770 775 780

Gly Ser Ser Ala Ala Tyr His Val Gly Val Asn Tyr Glu Trp Leu Glu
785 790 795 800

His His His His His His
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<210> 144
<211> 2256
<212> DNA
<213> Artificial Sequence

<220>
<223> ORF46.1-961c

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ctcaaagact atgccgcagc agccatccgc gattgggcag tccaaaaccc caatgccgca 840

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atgggcgcga tcgcattgcc gaaagggaaa tccgccgtca gcgacaattt tgccgatgcg    1020
gcatacgcca aatacccgtc cccttaccat tcccgaaata tccgttcaaa cttggagcag    1080
cgttacggca aagaaaacat cacctcctca accgtgccgc cgtcaaacgg caaaaatgtc    1140
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aattttgaga agcacgtgaa atatgatacg ggatccggag gaggaggagc cacaaacgac    1260
gacgatgtta aaaaagctgc cactgtggcc attgctgctg cctacaacaa tggccaagaa    1320
atcaacggtt tcaaagctgg agagaccatc tacgacattg atgaagacgg cacaattacc    1380
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gctttagcag atactgatgc cgctctggat gcaaccacca acgccttgaa taaattggga    1620
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gtcgctgcaa aagttaccga catcaaagct gatatcgcta cgaacaaaga taatattgct    1980
aaaaaagcaa acagtgccga cgtgtacacc agagaagagt ctgacagcaa atttgtcaga    2040
attgatggtc tgaacgctac taccgaaaaa ttggacacac gcttggcttc tgctgaaaaa    2100
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aaagaaaccc gccaaggcct tgcagaacaa gccgcgctct ccggtctgtt ccaaccttac    2220
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<210> 145
<211> 751
<212> PRT
<213> Artificial Sequence

<220>
<223> ORF46.1-961c

<400> 145

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Gln His Phe Glu Pro Asp Gly Lys Tyr His Leu Phe Gly Ser Arg Gly
            20                  25                  30

Glu Leu Ala Glu Arg Ser Gly His Ile Gly Leu Gly Lys Ile Gln Ser
        35                  40                  45

His Gln Leu Gly Asn Leu Met Ile Gln Gln Ala Ala Ile Lys Gly Asn
    50                  55                  60

Ile Gly Tyr Ile Val Arg Phe Ser Asp His Gly His Glu Val His Ser
65                  70                  75                  80

Pro Phe Asp Asn His Ala Ser His Ser Asp Ser Asp Glu Ala Gly Ser
                85                  90                  95

Pro Val Asp Gly Phe Ser Leu Tyr Arg Ile His Trp Asp Gly Tyr Glu
            100                 105                 110

His His Pro Ala Asp Gly Tyr Asp Gly Pro Gln Gly Gly Gly Tyr Pro
        115                 120                 125

Ala Pro Lys Gly Ala Arg Asp Ile Tyr Ser Tyr Asp Ile Lys Gly Val
    130                 135                 140

Ala Gln Asn Ile Arg Leu Asn Leu Thr Asp Asn Arg Ser Thr Gly Gln
145                 150                 155                 160

Arg Leu Ala Asp Arg Phe His Asn Ala Gly Ser Met Leu Thr Gln Gly
                165                 170                 175

Val Gly Asp Gly Phe Lys Arg Ala Thr Arg Tyr Ser Pro Glu Leu Asp
            180                 185                 190
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Arg Ser Gly Asn Ala Ala Glu Ala Phe Asn Gly Thr Ala Asp Ile Val
195 200 205

Lys Asn Ile Ile Gly Ala Ala Gly Glu Ile Val Gly Ala Gly Asp Ala
210 215 220

Val Gln Gly Ile Ser Glu Gly Ser Asn Ile Ala Val Met His Gly Leu
225 230 235 240

Gly Leu Leu Ser Thr Glu Asn Lys Met Ala Arg Ile Asn Asp Leu Ala
245 250 255

Asp Met Ala Gln Leu Lys Asp Tyr Ala Ala Ala Ala Ile Arg Asp Trp
260 265 270

Ala Val Gln Asn Pro Asn Ala Ala Gln Gly Ile Glu Ala Val Ser Asn
275 280 285

Ile Phe Met Ala Ala Ile Pro Ile Lys Gly Ile Gly Ala Val Arg Gly
290 295 300

Lys Tyr Gly Leu Gly Gly Ile Thr Ala His Pro Ile Lys Arg Ser Gln
305 310 315 320

Met Gly Ala Ile Ala Leu Pro Lys Gly Lys Ser Ala Val Ser Asp Asn
325 330 335

Phe Ala Asp Ala Ala Tyr Ala Lys Tyr Pro Ser Pro Tyr His Ser Arg
340 345 350

Asn Ile Arg Ser Asn Leu Glu Gln Arg Tyr Gly Lys Glu Asn Ile Thr
355 360 365

Ser Ser Thr Val Pro Pro Ser Asn Gly Lys Asn Val Lys Leu Ala Asp
370 375 380

Gln Arg His Pro Lys Thr Gly Val Pro Phe Asp Gly Lys Gly Phe Pro
385 390 395 400

Asn Phe Glu Lys His Val Lys Tyr Asp Thr Gly Ser Gly Gly Gly Gly
405 410 415

Ala Thr Asn Asp Asp Asp Val Lys Lys Ala Ala Thr Val Ala Ile Ala
420 425 430

Ala Ala Tyr Asn Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala Gly Glu
435 440 445

Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp Ala
450 455 460

Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu Lys
465 470 475 480

Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys Gln Asn
485 490 495

Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu Thr
500 505 510

Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala Ala
515 520 525

Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile Thr
530 535 540

Thr Phe Ala Glu Glu Thr Lys Thr Asn Ile Val Lys Ile Asp Glu Lys
545 550 555 560

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Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala Phe Asn
                565                 570                 575

Asp Ile Ala Asp Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp Glu Ala
            580                 585                 590

Val Lys Thr Ala Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr Lys Gln
        595                 600                 605

Asn Val Asp Ala Lys Val Lys Ala Ala Glu Thr Ala Ala Gly Lys Ala
    610                 615                 620

Glu Ala Ala Ala Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala Glu Ala
625                 630                 635                 640

Val Ala Ala Lys Val Thr Asp Ile Lys Ala Asp Ile Ala Thr Asn Lys
                645                 650                 655

Asp Asn Ile Ala Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr Arg Glu
            660                 665                 670

Glu Ser Asp Ser Lys Phe Val Arg Ile Asp Gly Leu Asn Ala Thr Thr
        675                 680                 685

Glu Lys Leu Asp Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile Ala Asp
    690                 695                 700

His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp Leu Arg
705                 710                 715                 720

Lys Glu Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly Leu
                725                 730                 735

Phe Gln Pro Tyr Asn Val Gly Leu Glu His His His His His His
            740                 745                 750

<210>   146
<211>   2421
<212>   DNA
<213>   Artificial Sequence

<220>
<223>   961-ORF46.1

<400>   146
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gacggcacaa ttaccaaaaa agacgcaact gcagccgatg ttgaagccga cgactttaaa     180
ggtctgggtc tgaaaaaagt cgtgactaac ctgaccaaaa ccgtcaatga aaacaaacaa     240
aacgtcgatg ccaaagtaaa agctgcagaa tctgaaatag aaaagttaac aaccaagtta     300
gcagacactg atgccgcttt agcagatact gatgccgctc tggatgcaac caccaacgcc     360
ttgaataaat tgggagaaaa tataacgaca tttgctgaag agactaagac aaatatcgta     420
aaaattgatg aaaaattaga agccgtggct gataccgtcg acaagcatgc cgaagcattc     480
aacgatatcg ccgattcatt ggatgaaacc aacactaagg cagacgaagc cgtcaaaacc     540
gccaatgaag ccaaacagac ggccgaagaa accaaacaaa acgtcgatgc caaagtaaaa     600
gctgcagaaa ctgcagcagg caaagccgaa gctgccgctg gcacagctaa tactgcagcc     660
gacaaggccg aagctgtcgc tgcaaaagtt accgacatca aagctgatat cgctacgaac     720
aaagataata ttgctaaaaa agcaaacagt gccgacgtgt acaccagaga agagtctgac     780
agcaaatttg tcagaattga tggtctgaac gctactaccg aaaaattgga cacacgcttg     840
gcttctgctg aaaaatccat tgccgatcac gatactcgcc tgaacggttt ggataaaaca     900
gtgtcagacc tgcgcaaaga aacccgccaa ggccttgcag aacaagccgc gctctccggt     960
ctgttccaac cttacaacgt gggtcggttc aatgtaacgg ctgcagtcgg cggctacaaa    1020
tccgaatcgg cagtcgccat cggtaccggc ttccgcttta ccgaaaactt tgccgccaaa    1080
gcaggcgtgg cagtcggcac ttcgtccggt tcttccgcag cctaccatgt cggcgtcaat    1140
tacgagtggg gatccggagg aggaggatca gatttggcaa acgattcttt tatccggcag    1200
gttctcgacc gtcagcattt cgaacccgac gggaaatacc acctattcgg cagcaggggg    1260
gaacttgccg agcgcagcgg ccatatcgga ttgggaaaaa tacaaagcca tcagttgggc    1320
aacctgatga ttcaacaggc ggccattaaa ggaaatatcg gctacattgt ccgcttttcc    1380
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ccgccgtcaa acggcaaaaa tgtcaaactg gcagaccaac gccacccgaa gacaggcgta 2340
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caccaccacc accaccactg a 2421

<210> 147
<211> 806
<212> PRT
<213> Artificial Sequence

<220>
<223> 961-ORF46.1

<400> 147
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Ala Ala Ala Tyr Asn Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala Gly
20 25 30

Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp
35 40 45

Ala Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu
50 55 60

Lys Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys Gln
65 70 75 80

Asn Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu
85 90 95

Thr Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala
100 105 110

Ala Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile
115 120 125

Thr Thr Phe Ala Glu Glu Thr Lys Thr Asn Ile Val Lys Ile Asp Glu
130 135 140

Lys Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala Phe
145 150 155 160

Asn Asp Ile Ala Asp Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp Glu
165 170 175

Ala Val Lys Thr Ala Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr Lys
180 185 190

Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu Thr Ala Ala Gly Lys
195 200 205

Ala Glu Ala Ala Ala Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala Glu
210 215 220

Ala Val Ala Ala Lys Val Thr Asp Ile Lys Ala Asp Ile Ala Thr Asn
225 230 235 240

Lys Asp Asn Ile Ala Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr Arg
245 250 255

Glu Glu Ser Asp Ser Lys Phe Val Arg Ile Asp Gly Leu Asn Ala Thr
260 265 270

Thr Glu Lys Leu Asp Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile Ala
275 280 285

Asp His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp Leu
290 295 300

Arg Lys Glu Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly
305 310 315 320

Leu Phe Gln Pro Tyr Asn Val Gly Arg Phe Asn Val Thr Ala Ala Val
325 330 335

Gly Gly Tyr Lys Ser Glu Ser Ala Val Ala Ile Gly Thr Gly Phe Arg
340 345 350

Phe Thr Glu Asn Phe Ala Ala Lys Ala Gly Val Ala Val Gly Thr Ser
355 360 365

Ser Gly Ser Ser Ala Ala Tyr His Val Gly Val Asn Tyr Glu Trp Gly
370 375 380

Ser Gly Gly Gly Gly Ser Asp Leu Ala Asn Asp Ser Phe Ile Arg Gln
385 390 395 400

Val Leu Asp Arg Gln His Phe Glu Pro Asp Gly Lys Tyr His Leu Phe
405 410 415

Gly Ser Arg Gly Glu Leu Ala Glu Arg Ser Gly His Ile Gly Leu Gly
420 425 430

Lys Ile Gln Ser His Gln Leu Gly Asn Leu Met Ile Gln Gln Ala Ala
435 440 445

Ile Lys Gly Asn Ile Gly Tyr Ile Val Arg Phe Ser Asp His Gly His
450 455 460

Glu Val His Ser Pro Phe Asp Asn His Ala Ser His Ser Asp Ser Asp
465 470 475 480

Glu Ala Gly Ser Pro Val Asp Gly Phe Ser Leu Tyr Arg Ile His Trp
485 490 495

Asp Gly Tyr Glu His His Pro Ala Asp Gly Tyr Asp Gly Pro Gln Gly
500 505 510

Gly Gly Tyr Pro Ala Pro Lys Gly Ala Arg Asp Ile Tyr Ser Tyr Asp
515 520 525

Ile Lys Gly Val Ala Gln Asn Ile Arg Leu Asn Leu Thr Asp Asn Arg
530 535 540

Ser Thr Gly Gln Arg Leu Ala Asp Arg Phe His Asn Ala Gly Ser Met
545 550 555 560

Leu Thr Gln Gly Val Gly Asp Gly Phe Lys Arg Ala Thr Arg Tyr Ser
565 570 575

Pro Glu Leu Asp Arg Ser Gly Asn Ala Ala Glu Ala Phe Asn Gly Thr
580 585 590

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Ala Asp Ile Val Lys Asn Ile Ile Gly Ala Ala Gly Glu Ile Val Gly
        595                 600                 605

Ala Gly Asp Ala Val Gln Gly Ile Ser Glu Gly Ser Asn Ile Ala Val
    610                 615                 620

Met His Gly Leu Gly Leu Leu Ser Thr Glu Asn Lys Met Ala Arg Ile
625                 630                 635                     640

Asn Asp Leu Ala Asp Met Ala Gln Leu Lys Asp Tyr Ala Ala Ala Ala
                645                 650                 655

Ile Arg Asp Trp Ala Val Gln Asn Pro Asn Ala Ala Gln Gly Ile Glu
            660                 665                 670

Ala Val Ser Asn Ile Phe Met Ala Ala Ile Pro Ile Lys Gly Ile Gly
        675                 680                 685

Ala Val Arg Gly Lys Tyr Gly Leu Gly Gly Ile Thr Ala His Pro Ile
    690                 695                 700

Lys Arg Ser Gln Met Gly Ala Ile Ala Leu Pro Lys Gly Lys Ser Ala
705                 710                 715                     720

Val Ser Asp Asn Phe Ala Asp Ala Ala Tyr Ala Lys Tyr Pro Ser Pro
                725                 730                 735

Tyr His Ser Arg Asn Ile Arg Ser Asn Leu Glu Gln Arg Tyr Gly Lys
            740                 745                 750

Glu Asn Ile Thr Ser Ser Thr Val Pro Pro Ser Asn Gly Lys Asn Val
        755                 760                 765

Lys Leu Ala Asp Gln Arg His Pro Lys Thr Gly Val Pro Phe Asp Gly
    770                 775                 780

Lys Gly Phe Pro Asn Phe Glu Lys His Val Lys Tyr Asp Thr Leu Glu
785                 790                 795                     800

His His His His His His
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<210> 148
<211> 1938
<212> DNA
<213> Artificial Sequence

<220>
<223> 961-741

<400> 148

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gacggcacaa ttaccaaaaa agacgcaact gcagccgatg ttgaagccga cgactttaaa   180
ggtctgggtc tgaaaaaagt cgtgactaac ctgaccaaaa ccgtcaatga aaacaaacaa   240
aacgtcgatg ccaaagtaaa agctgcagaa tctgaaatag aaaagttaac aaccaagtta   300
gcagacactg atgccgcttt agcagatact gatgccgctc tggatgcaac caccaacgcc   360
ttgaataaat tgggagaaaa tataacgaca tttgctgaag agactaagac aaatatcgta   420
aaaattgatg aaaaattaga agccgtggct gataccgtcg acaagcatgc cgaagcattc   480
aacgatatcg ccgattcatt ggatgaaacc aacactaagg cagacgaagc cgtcaaaacc   540
gccaatgaag ccaaacagac ggccgaagaa accaaacaaa acgtcgatgc caaagtaaaa   600
gctgcagaaa ctgcagcagg caaagccgaa gctgccgctg gcacagctaa tactgcagcc   660
gacaaggccg aagctgtcgc tgcaaaagtt accgacatca aagctgatat cgctacgaac   720
aaagataata ttgctaaaaa agcaaacagt gccgacgtgt acaccagaga agagtctgac   780
agcaaatttg tcagaattga tggtctgaac gctactaccg aaaaattgga cacacgcttg   840
gcttctgctg aaaaatccat tgccgatcac gatactcgcc tgaacggttt ggataaaaca   900
gtgtcagacc tgcgcaaaga aacccgccaa ggccttgcag aacaagccgc gctctccggt   960
ctgttccaac cttacaacgt gggtcggttc aatgtaacgg ctgcagtcgg cggctacaaa  1020
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tccgaatcgg cagtcgccat cggtaccggc ttccgcttta ccgaaaactt tgccgccaaa   1080
gcaggcgtgg cagtcggcac ttcgtccggt tcttccgcag cctaccatgt cggcgtcaat   1140
tacgagtggg gatccggagg gggtggtgtc gccgccgaca tcggtgcggg gcttgccgat   1200
gcactaaccg caccgctcga ccataaagac aaaggtttgc agtctttgac gctggatcag   1260
tccgtcagga aaaacgagaa actgaagctg gcggcacaag gtgcggaaaa aacttatgga   1320
aacggtgaca gcctcaatac gggcaaattg aagaacgaca aggtcagccg tttcgacttt   1380
atccgccaaa tcgaagtgga cgggcagctc attaccttgg agagtggaga gttccaagta   1440
tacaaacaaa gccattccgc cttaaccgcc tttcagaccg agcaaataca agattcggag   1500
cattccggga agatggttgc gaaacgccag ttcagaatcg gcgacatagc gggcgaacat   1560
acatcttttg acaagcttcc cgaaggcggc agggcgacat atcgcgggac ggcgttcggt   1620
tcagacgatg ccggcggaaa actgacctac accatagatt tcgccgccaa gcagggaaac   1680
ggcaaaatcg aacatttgaa atcgccagaa ctcaatgtcg acctggccgc cgccgatatc   1740
aagccggatg gaaaacgcca tgccgtcatc agcggttccg tcctttacaa ccaagccgag   1800
aaaggcagtt actccctcgg tatctttggc ggaaaagccc aggaagttgc cggcagcgcg   1860
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<210> 149
<211> 645
<212> PRT
<213> Artificial Sequence

<220>
<223> 961-741

<400> 149

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Ala Ala Ala Tyr Asn Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala Gly
            20                  25                  30

Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp
        35                  40                  45

Ala Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu
    50                  55                  60

Lys Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys Gln
65                  70                  75                  80

Asn Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu
                85                  90                  95

Thr Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala
            100                 105                 110

Ala Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile
        115                 120                 125

Thr Thr Phe Ala Glu Glu Thr Lys Thr Asn Ile Val Lys Ile Asp Glu
    130                 135                 140

Lys Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala Phe
145                 150                 155                 160

Asn Asp Ile Ala Asp Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp Glu
                165                 170                 175

Ala Val Lys Thr Ala Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr Lys
            180                 185                 190

Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu Thr Ala Ala Gly Lys
        195                 200                 205

Ala Glu Ala Ala Ala Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala Glu
    210                 215                 220

Ala Val Ala Ala Lys Val Thr Asp Ile Lys Ala Asp Ile Ala Thr Asn
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225                 230                 235                 240

Lys Asp Asn Ile Ala Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr Arg
                245                 250                 255

Glu Glu Ser Asp Ser Lys Phe Val Arg Ile Asp Gly Leu Asn Ala Thr
            260                 265                 270

Thr Glu Lys Leu Asp Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile Ala
        275                 280                 285

Asp His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp Leu
    290                 295                 300

Arg Lys Glu Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly
305                 310                 315                 320

Leu Phe Gln Pro Tyr Asn Val Gly Arg Phe Asn Val Thr Ala Ala Val
                325                 330                 335

Gly Gly Tyr Lys Ser Glu Ser Ala Val Ala Ile Gly Thr Gly Phe Arg
            340                 345                 350

Phe Thr Glu Asn Phe Ala Ala Lys Ala Gly Val Ala Val Gly Thr Ser
        355                 360                 365

Ser Gly Ser Ser Ala Ala Tyr His Val Gly Val Asn Tyr Glu Trp Gly
    370                 375                 380

Ser Gly Gly Gly Gly Val Ala Ala Asp Ile Gly Ala Gly Leu Ala Asp
385                 390                 395                 400

Ala Leu Thr Ala Pro Leu Asp His Lys Asp Lys Gly Leu Gln Ser Leu
                405                 410                 415

Thr Leu Asp Gln Ser Val Arg Lys Asn Glu Lys Leu Lys Leu Ala Ala
            420                 425                 430

Gln Gly Ala Glu Lys Thr Tyr Gly Asn Gly Asp Ser Leu Asn Thr Gly
        435                 440                 445

Lys Leu Lys Asn Asp Lys Val Ser Arg Phe Asp Phe Ile Arg Gln Ile
    450                 455                 460

Glu Val Asp Gly Gln Leu Ile Thr Leu Glu Ser Gly Glu Phe Gln Val
465                 470                 475                 480

Tyr Lys Gln Ser His Ser Ala Leu Thr Ala Phe Gln Thr Glu Gln Ile
                485                 490                 495

Gln Asp Ser Glu His Ser Gly Lys Met Val Ala Lys Arg Gln Phe Arg
            500                 505                 510

Ile Gly Asp Ile Ala Gly Glu His Thr Ser Phe Asp Lys Leu Pro Glu
        515                 520                 525

Gly Gly Arg Ala Thr Tyr Arg Gly Thr Ala Phe Gly Ser Asp Asp Ala
    530                 535                 540

Gly Gly Lys Leu Thr Tyr Thr Ile Asp Phe Ala Ala Lys Gln Gly Asn
545                 550                 555                 560

Gly Lys Ile Glu His Leu Lys Ser Pro Glu Leu Asn Val Asp Leu Ala
                565                 570                 575

Ala Ala Asp Ile Lys Pro Asp Gly Lys Arg His Ala Val Ile Ser Gly
            580                 585                 590

Ser Val Leu Tyr Asn Gln Ala Glu Lys Gly Ser Tyr Ser Leu Gly Ile
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        595                 600                 605

Phe Gly Gly Lys Ala Gln Glu Val Ala Gly Ser Ala Glu Val Lys Thr
    610                 615                 620

Val Asn Gly Ile Arg His Ile Gly Leu Ala Ala Lys Gln Leu Glu His
625                 630                 635                 640

His His His His His
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<210> 150
<211> 4335
<212> DNA
<213> Artificial Sequence

<220>
<223> 961-983

<400> 150

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ggtctgggtc tgaaaaaagt cgtgactaac ctgaccaaaa ccgtcaatga aaacaaacaa   240
aacgtcgatg ccaaagtaaa agctgcagaa tctgaaatag aaaagttaac aaccaagtta   300
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gccaatgaag ccaaacagac ggccgaagaa accaaacaaa acgtcgatgc caaagtaaaa   600
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atccgtaata aaaacatgct tttcatcttt tcgacaggca atgacgcaca agctcagccc  2100
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tccggcgcaa acgaaaccgt acacatcaaa ggcagtctgc agctggacgg caaaggtacg  2880
ctgtacacac gtttgggcaa actgctgaaa gtggacggta cggcgattat cggcggcaag  2940
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gtctatgccg acagtaccgc cgcccatgcc gatatgcagg gacgccgcct gaaagccgta    3480
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gaacgcgacc tgaacggacg cgactacacg gtaacgggcg gctttaccgg cgcgactgca    4140
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gcggatgtcg aattcggcaa cggctggaac ggcttggcac gttacagcta cgccggttcc    4260
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<213> Artificial Sequence

<220>
<223> 961-983

<400> 151

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Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp
        35                  40                  45

Ala Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu
    50                  55                  60

Lys Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys Gln
65                  70                  75                  80

Asn Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu
                85                  90                  95

Thr Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala
            100                 105                 110

Ala Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile
        115                 120                 125

Thr Thr Phe Ala Glu Glu Thr Lys Thr Asn Ile Val Lys Ile Asp Glu
    130                 135                 140

Lys Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala Phe
145                 150                 155                 160

Asn Asp Ile Ala Asp Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp Glu
                165                 170                 175

Ala Val Lys Thr Ala Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr Lys
            180                 185                 190
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Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu Thr Ala Ala Gly Lys
195 200 205

Ala Glu Ala Ala Ala Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala Glu
210 215 220

Ala Val Ala Ala Lys Val Thr Asp Ile Lys Ala Asp Ile Ala Thr Asn
225 230 235 240

Lys Asp Asn Ile Ala Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr Arg
245 250 255

Glu Glu Ser Asp Ser Lys Phe Val Arg Ile Asp Gly Leu Asn Ala Thr
260 265 270

Thr Glu Lys Leu Asp Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile Ala
275 280 285

Asp His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp Leu
290 295 300

Arg Lys Glu Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly
305 310 315 320

Leu Phe Gln Pro Tyr Asn Val Gly Arg Phe Asn Val Thr Ala Ala Val
325 330 335

Gly Gly Tyr Lys Ser Glu Ser Ala Val Ala Ile Gly Thr Gly Phe Arg
340 345 350

Phe Thr Glu Asn Phe Ala Ala Lys Ala Gly Val Ala Val Gly Thr Ser
355 360 365

Ser Gly Ser Ser Ala Ala Tyr His Val Gly Val Asn Tyr Glu Trp Gly
370 375 380

Ser Gly Gly Gly Gly Thr Ser Ala Pro Asp Phe Asn Ala Gly Gly Thr
385 390 395 400

Gly Ile Gly Ser Asn Ser Arg Ala Thr Thr Ala Lys Ser Ala Ala Val
405 410 415

Ser Tyr Ala Gly Ile Lys Asn Glu Met Cys Lys Asp Arg Ser Met Leu
420 425 430

Cys Ala Gly Arg Asp Asp Val Ala Val Thr Asp Arg Asp Ala Lys Ile
435 440 445

Asn Ala Pro Pro Pro Asn Leu His Thr Gly Asp Phe Pro Asn Pro Asn
450 455 460

Asp Ala Tyr Lys Asn Leu Ile Asn Leu Lys Pro Ala Ile Glu Ala Gly
465 470 475 480

Tyr Thr Gly Arg Gly Val Glu Val Gly Ile Val Asp Thr Gly Glu Ser
485 490 495

Val Gly Ser Ile Ser Phe Pro Glu Leu Tyr Gly Arg Lys Glu His Gly
500 505 510

Tyr Asn Glu Asn Tyr Lys Asn Tyr Thr Ala Tyr Met Arg Lys Glu Ala
515 520 525

Pro Glu Asp Gly Gly Gly Lys Asp Ile Glu Ala Ser Phe Asp Asp Glu
530 535 540

Ala Val Ile Glu Thr Glu Ala Lys Pro Thr Asp Ile Arg His Val Lys
545 550 555 560

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Glu Ile Gly His Ile Asp Leu Val Ser His Ile Ile Gly Gly Arg Ser
                565                 570                 575

Val Asp Gly Arg Pro Ala Gly Gly Ile Ala Pro Asp Ala Thr Leu His
            580                 585                 590

Ile Met Asn Thr Asn Asp Glu Thr Lys Asn Glu Met Met Val Ala Ala
        595                 600                 605

Ile Arg Asn Ala Trp Val Lys Leu Gly Glu Arg Gly Val Arg Ile Val
    610                 615                 620

Asn Asn Ser Phe Gly Thr Thr Ser Arg Ala Gly Thr Ala Asp Leu Phe
625                 630                 635                 640

Gln Ile Ala Asn Ser Glu Glu Gln Tyr Arg Gln Ala Leu Leu Asp Tyr
                645                 650                 655

Ser Gly Gly Asp Lys Thr Asp Glu Gly Ile Arg Leu Met Gln Gln Ser
            660                 665                 670

Asp Tyr Gly Asn Leu Ser Tyr His Ile Arg Asn Lys Asn Met Leu Phe
        675                 680                 685

Ile Phe Ser Thr Gly Asn Asp Ala Gln Ala Gln Pro Asn Thr Tyr Ala
    690                 695                 700

Leu Leu Pro Phe Tyr Glu Lys Asp Ala Gln Lys Gly Ile Ile Thr Val
705                 710                 715                 720

Ala Gly Val Asp Arg Ser Gly Glu Lys Phe Lys Arg Glu Met Tyr Gly
                725                 730                 735

Glu Pro Gly Thr Glu Pro Leu Glu Tyr Gly Ser Asn His Cys Gly Ile
            740                 745                 750

Thr Ala Met Trp Cys Leu Ser Ala Pro Tyr Glu Ala Ser Val Arg Phe
        755                 760                 765

Thr Arg Thr Asn Pro Ile Gln Ile Ala Gly Thr Ser Phe Ser Ala Pro
    770                 775                 780

Ile Val Thr Gly Thr Ala Ala Leu Leu Leu Gln Lys Tyr Pro Trp Met
785                 790                 795                 800

Ser Asn Asp Asn Leu Arg Thr Thr Leu Leu Thr Thr Ala Gln Asp Ile
                805                 810                 815

Gly Ala Val Gly Val Asp Ser Lys Phe Gly Trp Gly Leu Leu Asp Ala
            820                 825                 830

Gly Lys Ala Met Asn Gly Pro Ala Ser Phe Pro Phe Gly Asp Phe Thr
        835                 840                 845

Ala Asp Thr Lys Gly Thr Ser Asp Ile Ala Tyr Ser Phe Arg Asn Asp
    850                 855                 860

Ile Ser Gly Thr Gly Gly Leu Ile Lys Lys Gly Gly Ser Gln Leu Gln
865                 870                 875                 880

Leu His Gly Asn Asn Thr Tyr Thr Gly Lys Thr Ile Ile Glu Gly Gly
                885                 890                 895

Ser Leu Val Leu Tyr Gly Asn Asn Lys Ser Asp Met Arg Val Glu Thr
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Lys Gly Ala Leu Ile Tyr Asn Gly Ala Ala Ser Gly Gly Ser Leu Asn
        915                 920                 925
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Ser Asp Gly Ile Val Tyr Leu Ala Asp Thr Asp Gln Ser Gly Ala Asn
    930                 935                 940

Glu Thr Val His Ile Lys Gly Ser Leu Gln Leu Asp Gly Lys Gly Thr
945                 950                 955                 960

Leu Tyr Thr Arg Leu Gly Lys Leu Leu Lys Val Asp Gly Thr Ala Ile
                965                 970                 975

Ile Gly Gly Lys Leu Tyr Met Ser Ala Arg Gly Lys Gly Ala Gly Tyr
            980                 985                 990

Leu Asn Ser Thr Gly Arg Arg Val Pro Phe Leu Ser Ala Ala Lys Ile
        995                 1000                1005

Gly Gln Asp Tyr Ser Phe Phe Thr Asn Ile Glu Thr Asp Gly Gly Leu
    1010                1015                1020

Leu Ala Ser Leu Asp Ser Val Glu Lys Thr Ala Gly Ser Glu Gly Asp
1025                1030                1035                1040

Thr Leu Ser Tyr Tyr Val Arg Arg Gly Asn Ala Ala Arg Thr Ala Ser
                1045                1050                1055

Ala Ala Ala His Ser Ala Pro Ala Gly Leu Lys His Ala Val Glu Gln
            1060                1065                1070

Gly Gly Ser Asn Leu Glu Asn Leu Met Val Glu Leu Asp Ala Ser Glu
        1075                1080                1085

Ser Ser Ala Thr Pro Glu Thr Val Glu Thr Ala Ala Ala Asp Arg Thr
    1090                1095                1100

Asp Met Pro Gly Ile Arg Pro Tyr Gly Ala Thr Phe Arg Ala Ala Ala
1105                1110                1115                1120

Ala Val Gln His Ala Asn Ala Ala Asp Gly Val Arg Ile Phe Asn Ser
                1125                1130                1135

Leu Ala Ala Thr Val Tyr Ala Asp Ser Thr Ala Ala His Ala Asp Met
            1140                1145                1150

Gln Gly Arg Arg Leu Lys Ala Val Ser Asp Gly Leu Asp His Asn Gly
        1155                1160                1165

Thr Gly Leu Arg Val Ile Ala Gln Thr Gln Gln Asp Gly Gly Thr Trp
    1170                1175                1180

Glu Gln Gly Gly Val Glu Gly Lys Met Arg Gly Ser Thr Gln Thr Val
1185                1190                1195                1200

Gly Ile Ala Ala Lys Thr Gly Glu Asn Thr Thr Ala Ala Ala Thr Leu
                1205                1210                1215

Gly Met Gly Arg Ser Thr Trp Ser Glu Asn Ser Ala Asn Ala Lys Thr
            1220                1225                1230

Asp Ser Ile Ser Leu Phe Ala Gly Ile Arg His Asp Ala Gly Asp Ile
        1235                1240                1245

Gly Tyr Leu Lys Gly Leu Phe Ser Tyr Gly Arg Tyr Lys Asn Ser Ile
    1250                1255                1260

Ser Arg Ser Thr Gly Ala Asp Glu His Ala Glu Gly Ser Val Asn Gly
1265                1270                1275                1280

Thr Leu Met Gln Leu Gly Ala Leu Gly Gly Val Asn Val Pro Phe Ala
                1285                1290                1295
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Ala Thr Gly Asp Leu Thr Val Glu Gly Gly Leu Arg Tyr Asp Leu Leu
1300 1305 1310

Lys Gln Asp Ala Phe Ala Glu Lys Gly Ser Ala Leu Gly Trp Ser Gly
1315 1320 1325

Asn Ser Leu Thr Glu Gly Thr Leu Val Gly Leu Ala Gly Leu Lys Leu
1330 1335 1340

Ser Gln Pro Leu Ser Asp Lys Ala Val Leu Phe Ala Thr Ala Gly Val
1345 1350 1355 1360

Glu Arg Asp Leu Asn Gly Arg Asp Tyr Thr Val Thr Gly Gly Phe Thr
1365 1370 1375

Gly Ala Thr Ala Ala Thr Gly Lys Thr Gly Ala Arg Asn Met Pro His
1380 1385 1390

Thr Arg Leu Val Ala Gly Leu Gly Ala Asp Val Glu Phe Gly Asn Gly
1395 1400 1405

Trp Asn Gly Leu Ala Arg Tyr Ser Tyr Ala Gly Ser Lys Gln Tyr Gly
1410 1415 1420

Asn His Ser Gly Arg Val Gly Val Gly Tyr Arg Phe Leu Glu His His
1425 1430 1435 1440

His His His His

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<211> 2256
<212> DNA
<213> Artificial Sequence

<220>
<223> 961c-ORF46.1

<400> 152
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gacggcacaa ttaccaaaaa agacgcaact gcagccgatg ttgaagccga cgactttaaa 180
ggtctgggtc tgaaaaaagt cgtgactaac ctgaccaaaa ccgtcaatga aaacaaacaa 240
aacgtcgatg ccaaagtaaa agctgcagaa tctgaaatag aaaagttaac aaccaagtta 300
gcagacactg atgccgcttt agcagatact gatgccgctc tggatgcaac caccaacgcc 360
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aacgatatcg ccgattcatt ggatgaaacc aacactaagg cagacgaagc cgtcaaaacc 540
gccaatgaag ccaaacagac ggccgaagaa accaaacaaa acgtcgatgc caaagtaaaa 600
gctgcagaaa ctgcagcagg caaagccgaa gctgccgctg gcacagctaa tactgcagcc 660
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ataagcgaag gctcaaacat tgctgtcatg cacggcttgg gtctgctttc caccgaaaac 1740

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aatatcttta tggcagccat ccccatcaaa gggattggag ctgttcgggg aaaatacggc    1920
ttgggcggca tcacggcaca tcctatcaag cggtcgcaga tgggcgcgat cgcattgccg    1980
aaagggaaat ccgccgtcag cgacaatttt gccgatgcgg catacgccaa atacccgtcc    2040
ccttaccatt cccgaaatat ccgttcaaac ttggagcagc gttacggcaa agaaaacatc    2100
acctcctcaa ccgtgccgcc gtcaaacggc aaaaatgtca aactggcaga ccaacgccac    2160
ccgaagacag gcgtaccgtt tgacggtaaa gggtttccga attttgagaa gcacgtgaaa    2220
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&lt;210&gt;   153
&lt;211&gt;   751
&lt;212&gt;   PRT
&lt;213&gt;   Artificial Sequence

&lt;220&gt;
&lt;223&gt;   961c-ORF46.1

&lt;400&gt;   153
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Ala Ala Ala Tyr Asn Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala Gly
            20                  25                  30

Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp
        35                  40                  45

Ala Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu
    50                  55                  60

Lys Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys Gln
65                  70                  75                  80

Asn Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu
                85                  90                  95

Thr Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala
            100                 105                 110

Ala Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile
        115                 120                 125

Thr Thr Phe Ala Glu Glu Thr Lys Thr Asn Ile Val Lys Ile Asp Glu
    130                 135                 140

Lys Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala Phe
145                 150                 155                 160

Asn Asp Ile Ala Asp Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp Glu
                165                 170                 175

Ala Val Lys Thr Ala Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr Lys
            180                 185                 190

Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu Thr Ala Ala Gly Lys
        195                 200                 205

Ala Glu Ala Ala Ala Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala Glu
    210                 215                 220

Ala Val Ala Ala Lys Val Thr Asp Ile Lys Ala Asp Ile Ala Thr Asn
225                 230                 235                 240

Lys Asp Asn Ile Ala Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr Arg
                245                 250                 255

Glu Glu Ser Asp Ser Lys Phe Val Arg Ile Asp Gly Leu Asn Ala Thr
            260                 265                 270
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Thr Glu Lys Leu Asp Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile Ala
        275                 280                 285

Asp His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp Leu
    290                 295                 300

Arg Lys Glu Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly
305                 310                 315                 320

Leu Phe Gln Pro Tyr Asn Val Gly Gly Ser Gly Gly Gly Gly Ser Asp
                325                 330                 335

Leu Ala Asn Asp Ser Phe Ile Arg Gln Val Leu Asp Arg Gln His Phe
            340                 345                 350

Glu Pro Asp Gly Lys Tyr His Leu Phe Gly Ser Arg Gly Glu Leu Ala
        355                 360                 365

Glu Arg Ser Gly His Ile Gly Leu Gly Lys Ile Gln Ser His Gln Leu
    370                 375                 380

Gly Asn Leu Met Ile Gln Gln Ala Ala Ile Lys Gly Asn Ile Gly Tyr
385                 390                 395                 400

Ile Val Arg Phe Ser Asp His Gly His Glu Val His Ser Pro Phe Asp
                405                 410                 415

Asn His Ala Ser His Ser Asp Ser Asp Glu Ala Gly Ser Pro Val Asp
            420                 425                 430

Gly Phe Ser Leu Tyr Arg Ile His Trp Asp Gly Tyr Glu His His Pro
        435                 440                 445

Ala Asp Gly Tyr Asp Gly Pro Gln Gly Gly Gly Tyr Pro Ala Pro Lys
    450                 455                 460

Gly Ala Arg Asp Ile Tyr Ser Tyr Asp Ile Lys Gly Val Ala Gln Asn
465                 470                 475                 480

Ile Arg Leu Asn Leu Thr Asp Asn Arg Ser Thr Gly Gln Arg Leu Ala
                485                 490                 495

Asp Arg Phe His Asn Ala Gly Ser Met Leu Thr Gln Gly Val Gly Asp
            500                 505                 510

Gly Phe Lys Arg Ala Thr Arg Tyr Ser Pro Glu Leu Asp Arg Ser Gly
        515                 520                 525

Asn Ala Ala Glu Ala Phe Asn Gly Thr Ala Asp Ile Val Lys Asn Ile
    530                 535                 540

Ile Gly Ala Ala Gly Glu Ile Val Gly Ala Gly Asp Ala Val Gln Gly
545                 550                 555                 560

Ile Ser Glu Gly Ser Asn Ile Ala Val Met His Gly Leu Gly Leu Leu
                565                 570                 575

Ser Thr Glu Asn Lys Met Ala Arg Ile Asn Asp Leu Ala Asp Met Ala
            580                 585                 590

Gln Leu Lys Asp Tyr Ala Ala Ala Ala Ile Arg Asp Trp Ala Val Gln
        595                 600                 605

Asn Pro Asn Ala Ala Gln Gly Ile Glu Ala Val Ser Asn Ile Phe Met
    610                 615                 620

Ala Ala Ile Pro Ile Lys Gly Ile Gly Ala Val Arg Gly Lys Tyr Gly
625                 630                 635                 640
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Leu Gly Gly Ile Thr Ala His Pro Ile Lys Arg Ser Gln Met Gly Ala
645 650 655

Ile Ala Leu Pro Lys Gly Lys Ser Ala Val Ser Asp Asn Phe Ala Asp
660 665 670

Ala Ala Tyr Ala Lys Tyr Pro Ser Pro Tyr His Ser Arg Asn Ile Arg
675 680 685

Ser Asn Leu Glu Gln Arg Tyr Gly Lys Glu Asn Ile Thr Ser Ser Thr
690 695 700

Val Pro Pro Ser Asn Gly Lys Asn Val Lys Leu Ala Asp Gln Arg His
705 710 715 720

Pro Lys Thr Gly Val Pro Phe Asp Gly Lys Gly Phe Pro Asn Phe Glu
725 730 735

Lys His Val Lys Tyr Asp Thr Leu Glu His His His His His His
740 745 750

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<211> 1773
<212> DNA
<213> Artificial Sequence

<220>
<223> 961c-741

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gacggcacaa ttaccaaaaa agacgcaact gcagccgatg ttgaagccga cgactttaaa 180
ggtctgggtc tgaaaaaagt cgtgactaac ctgaccaaaa ccgtcaatga aaacaaacaa 240
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gccaatgaag ccaaacagac ggccgaagaa accaaacaaa acgtcgatgc caaagtaaaa 600
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gccgccgccg atatcaagcc ggatggaaaa cgccatgccg tcatcagcgg ttccgtcctt 1620
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<211> 590
<212> PRT
<213> Artificial Sequence

<220>
<223> 961c-741

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20 25 30

Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp
35 40 45

Ala Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu
50 55 60

Lys Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys Gln
65 70 75 80

Asn Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu
85 90 95

Thr Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala
100 105 110

Ala Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile
115 120 125

Thr Thr Phe Ala Glu Glu Thr Lys Thr Asn Ile Val Lys Ile Asp Glu
130 135 140

Lys Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala Phe
145 150 155 160

Asn Asp Ile Ala Asp Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp Glu
165 170 175

Ala Val Lys Thr Ala Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr Lys
180 185 190

Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu Thr Ala Ala Gly Lys
195 200 205

Ala Glu Ala Ala Ala Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala Glu
210 215 220

Ala Val Ala Ala Lys Val Thr Asp Ile Lys Ala Asp Ile Ala Thr Asn
225 230 235 240

Lys Asp Asn Ile Ala Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr Arg
245 250 255

Glu Glu Ser Asp Ser Lys Phe Val Arg Ile Asp Gly Leu Asn Ala Thr
260 265 270

Thr Glu Lys Leu Asp Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile Ala
275 280 285

Asp His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp Leu
290 295 300

Arg Lys Glu Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly
305 310 315 320

Leu Phe Gln Pro Tyr Asn Val Gly Gly Ser Gly Gly Gly Gly Val Ala
325 330 335

Ala Asp Ile Gly Ala Gly Leu Ala Asp Ala Leu Thr Ala Pro Leu Asp
340 345 350

His Lys Asp Lys Gly Leu Gln Ser Leu Thr Leu Asp Gln Ser Val Arg

355 360 365

Lys Asn Glu Lys Leu Lys Leu Ala Ala Gln Gly Ala Glu Lys Thr Tyr
370 375 380

Gly Asn Gly Asp Ser Leu Asn Thr Gly Lys Leu Lys Asn Asp Lys Val
385 390 395 400

Ser Arg Phe Asp Phe Ile Arg Gln Ile Glu Val Asp Gly Gln Leu Ile
405 410 415

Thr Leu Glu Ser Gly Glu Phe Gln Val Tyr Lys Gln Ser His Ser Ala
420 425 430

Leu Thr Ala Phe Gln Thr Glu Gln Ile Gln Asp Ser Glu His Ser Gly
435 440 445

Lys Met Val Ala Lys Arg Gln Phe Arg Ile Gly Asp Ile Ala Gly Glu
450 455 460

His Thr Ser Phe Asp Lys Leu Pro Glu Gly Gly Arg Ala Thr Tyr Arg
465 470 475 480

Gly Thr Ala Phe Gly Ser Asp Asp Ala Gly Gly Lys Leu Thr Tyr Thr
485 490 495

Ile Asp Phe Ala Ala Lys Gln Gly Asn Gly Lys Ile Glu His Leu Lys
500 505 510

Ser Pro Glu Leu Asn Val Asp Leu Ala Ala Ala Asp Ile Lys Pro Asp
515 520 525

Gly Lys Arg His Ala Val Ile Ser Gly Ser Val Leu Tyr Asn Gln Ala
530 535 540

Glu Lys Gly Ser Tyr Ser Leu Gly Ile Phe Gly Gly Lys Ala Gln Glu
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Val Ala Gly Ser Ala Glu Val Lys Thr Val Asn Gly Ile Arg His Ile
565 570 575

Gly Leu Ala Ala Lys Gln Leu Glu His His His His His His
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<223> 961c-983

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aatctggaaa acctgatggt cgaactggat gcctccgaat catccgcaac acccgagacg    3120
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cgcctgaaag ccgtatcgga cgggttggac cacaacggca cgggtctgcg cgtcatcgcg    3360
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agtacccaaa ccgtcggcat tgccgcgaaa accggcgaaa atacgacagc agccgccaca    3480
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gcaacggcgg gcgtggaacg cgacctgaac ggacgcgact acacggtaac gggcggcttt    3960
accggcgcga ctgcagcaac cggcaagacg gggcacgca atatgccgca cacccgtctg    4020
gttgccggcc tgggcgcgga tgtcgaattc ggcaacggct ggaacggctt ggcacgttac    4080
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<210> 157
<211> 1389
<212> PRT
<213> Artificial Sequence

<220>
<223> 961c-983

<400> 157

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Ala Ala Ala Tyr Asn Asn Gly Gln Glu Ile Asn Gly Phe Lys Ala Gly
            20                  25                  30
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Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly Thr Ile Thr Lys Lys Asp
35 40 45

Ala Thr Ala Ala Asp Val Glu Ala Asp Asp Phe Lys Gly Leu Gly Leu
50 55 60

Lys Lys Val Val Thr Asn Leu Thr Lys Thr Val Asn Glu Asn Lys Gln
65 70 75 80

Asn Val Asp Ala Lys Val Lys Ala Ala Glu Ser Glu Ile Glu Lys Leu
85 90 95

Thr Thr Lys Leu Ala Asp Thr Asp Ala Ala Leu Ala Asp Thr Asp Ala
100 105 110

Ala Leu Asp Ala Thr Thr Asn Ala Leu Asn Lys Leu Gly Glu Asn Ile
115 120 125

Thr Thr Phe Ala Glu Glu Thr Lys Thr Asn Ile Val Lys Ile Asp Glu
130 135 140

Lys Leu Glu Ala Val Ala Asp Thr Val Asp Lys His Ala Glu Ala Phe
145 150 155 160

Asn Asp Ile Ala Asp Ser Leu Asp Glu Thr Asn Thr Lys Ala Asp Glu
165 170 175

Ala Val Lys Thr Ala Asn Glu Ala Lys Gln Thr Ala Glu Glu Thr Lys
180 185 190

Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu Thr Ala Ala Gly Lys
195 200 205

Ala Glu Ala Ala Ala Gly Thr Ala Asn Thr Ala Ala Asp Lys Ala Glu
210 215 220

Ala Val Ala Ala Lys Val Thr Asp Ile Lys Ala Asp Ile Ala Thr Asn
225 230 235 240

Lys Asp Asn Ile Ala Lys Lys Ala Asn Ser Ala Asp Val Tyr Thr Arg
245 250 255

Glu Glu Ser Asp Ser Lys Phe Val Arg Ile Asp Gly Leu Asn Ala Thr
260 265 270

Thr Glu Lys Leu Asp Thr Arg Leu Ala Ser Ala Glu Lys Ser Ile Ala
275 280 285

Asp His Asp Thr Arg Leu Asn Gly Leu Asp Lys Thr Val Ser Asp Leu
290 295 300

Arg Lys Glu Thr Arg Gln Gly Leu Ala Glu Gln Ala Ala Leu Ser Gly
305 310 315 320

Leu Phe Gln Pro Tyr Asn Val Gly Gly Ser Gly Gly Gly Gly Thr Ser
325 330 335

Ala Pro Asp Phe Asn Ala Gly Gly Thr Gly Ile Gly Ser Asn Ser Arg
340 345 350

Ala Thr Thr Ala Lys Ser Ala Ala Val Ser Tyr Ala Gly Ile Lys Asn
355 360 365

Glu Met Cys Lys Asp Arg Ser Met Leu Cys Ala Gly Arg Asp Asp Val
370 375 380

Ala Val Thr Asp Arg Asp Ala Lys Ile Asn Ala Pro Pro Pro Asn Leu
385 390 395 400

His Thr Gly Asp Phe Pro Asn Pro Asn Asp Ala Tyr Lys Asn Leu Ile
405 410 415

Asn Leu Lys Pro Ala Ile Glu Ala Gly Tyr Thr Gly Arg Gly Val Glu
420 425 430

Val Gly Ile Val Asp Thr Gly Glu Ser Val Gly Ser Ile Ser Phe Pro
435 440 445

Glu Leu Tyr Gly Arg Lys Glu His Gly Tyr Asn Glu Asn Tyr Lys Asn
450 455 460

Tyr Thr Ala Tyr Met Arg Lys Glu Ala Pro Glu Asp Gly Gly Gly Lys
465 470 475 480

Asp Ile Glu Ala Ser Phe Asp Asp Glu Ala Val Ile Glu Thr Glu Ala
485 490 495

Lys Pro Thr Asp Ile Arg His Val Lys Glu Ile Gly His Ile Asp Leu
500 505 510

Val Ser His Ile Ile Gly Gly Arg Ser Val Asp Gly Arg Pro Ala Gly
515 520 525

Gly Ile Ala Pro Asp Ala Thr Leu His Ile Met Asn Thr Asn Asp Glu
530 535 540

Thr Lys Asn Glu Met Met Val Ala Ala Ile Arg Asn Ala Trp Val Lys
545 550 555 560

Leu Gly Glu Arg Gly Val Arg Ile Val Asn Asn Ser Phe Gly Thr Thr
565 570 575

Ser Arg Ala Gly Thr Ala Asp Leu Phe Gln Ile Ala Asn Ser Glu Glu
580 585 590

Gln Tyr Arg Gln Ala Leu Leu Asp Tyr Ser Gly Gly Asp Lys Thr Asp
595 600 605

Glu Gly Ile Arg Leu Met Gln Gln Ser Asp Tyr Gly Asn Leu Ser Tyr
610 615 620

His Ile Arg Asn Lys Asn Met Leu Phe Ile Phe Ser Thr Gly Asn Asp
625 630 635 640

Ala Gln Ala Gln Pro Asn Thr Tyr Ala Leu Leu Pro Phe Tyr Glu Lys
645 650 655

Asp Ala Gln Lys Gly Ile Ile Thr Val Ala Gly Val Asp Arg Ser Gly
660 665 670

Glu Lys Phe Lys Arg Glu Met Tyr Gly Glu Pro Gly Thr Glu Pro Leu
675 680 685

Glu Tyr Gly Ser Asn His Cys Gly Ile Thr Ala Met Trp Cys Leu Ser
690 695 700

Ala Pro Tyr Glu Ala Ser Val Arg Phe Thr Arg Thr Asn Pro Ile Gln
705 710 715 720

Ile Ala Gly Thr Ser Phe Ser Ala Pro Ile Val Thr Gly Thr Ala Ala
725 730 735

Leu Leu Leu Gln Lys Tyr Pro Trp Met Ser Asn Asp Asn Leu Arg Thr
740 745 750

Thr Leu Leu Thr Thr Ala Gln Asp Ile Gly Ala Val Gly Val Asp Ser
755 760 765

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Lys Phe Gly Trp Gly Leu Leu Asp Ala Gly Lys Ala Met Asn Gly Pro
    770                 775                 780

Ala Ser Phe Pro Phe Gly Asp Phe Thr Ala Asp Thr Lys Gly Thr Ser
785                 790                 795                 800

Asp Ile Ala Tyr Ser Phe Arg Asn Asp Ile Ser Gly Thr Gly Gly Leu
                805                 810                 815

Ile Lys Lys Gly Gly Ser Gln Leu Gln Leu His Gly Asn Asn Thr Tyr
            820                 825                 830

Thr Gly Lys Thr Ile Ile Glu Gly Gly Ser Leu Val Leu Tyr Gly Asn
        835                 840                 845

Asn Lys Ser Asp Met Arg Val Glu Thr Lys Gly Ala Leu Ile Tyr Asn
    850                 855                 860

Gly Ala Ala Ser Gly Gly Ser Leu Asn Ser Asp Gly Ile Val Tyr Leu
865                 870                 875                 880

Ala Asp Thr Asp Gln Ser Gly Ala Asn Glu Thr Val His Ile Lys Gly
                885                 890                 895

Ser Leu Gln Leu Asp Gly Lys Gly Thr Leu Tyr Thr Arg Leu Gly Lys
            900                 905                 910

Leu Leu Lys Val Asp Gly Thr Ala Ile Ile Gly Gly Lys Leu Tyr Met
        915                 920                 925

Ser Ala Arg Gly Lys Gly Ala Gly Tyr Leu Asn Ser Thr Gly Arg Arg
    930                 935                 940

Val Pro Phe Leu Ser Ala Ala Lys Ile Gly Gln Asp Tyr Ser Phe Phe
945                 950                 955                 960

Thr Asn Ile Glu Thr Asp Gly Gly Leu Leu Ala Ser Leu Asp Ser Val
                965                 970                 975

Glu Lys Thr Ala Gly Ser Glu Gly Asp Thr Leu Ser Tyr Tyr Val Arg
            980                 985                 990

Arg Gly Asn Ala Ala Arg Thr Ala Ser Ala Ala Ala His Ser Ala Pro
        995                 1000                1005

Ala Gly Leu Lys His Ala Val Glu Gln Gly Gly Ser Asn Leu Glu Asn
    1010                1015                1020

Leu Met Val Glu Leu Asp Ala Ser Glu Ser Ser Ala Thr Pro Glu Thr
1025                1030                1035                1040

Val Glu Thr Ala Ala Ala Asp Arg Thr Asp Met Pro Gly Ile Arg Pro
                1045                1050                1055

Tyr Gly Ala Thr Phe Arg Ala Ala Ala Ala Val Gln His Ala Asn Ala
            1060                1065                1070

Ala Asp Gly Val Arg Ile Phe Asn Ser Leu Ala Ala Thr Val Tyr Ala
        1075                1080                1085

Asp Ser Thr Ala Ala His Ala Asp Met Gln Gly Arg Arg Leu Lys Ala
    1090                1095                1100

Val Ser Asp Gly Leu Asp His Asn Gly Thr Gly Leu Arg Val Ile Ala
1105                1110                1115                1120

Gln Thr Gln Gln Asp Gly Gly Thr Trp Glu Gln Gly Gly Val Glu Gly
                1125                1130                1135
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Lys Met Arg Gly Ser Thr Gln Thr Val Gly Ile Ala Ala Lys Thr Gly
1140 1145 1150

Glu Asn Thr Thr Ala Ala Ala Thr Leu Gly Met Gly Arg Ser Thr Trp
1155 1160 1165

Ser Glu Asn Ser Ala Asn Ala Lys Thr Asp Ser Ile Ser Leu Phe Ala
1170 1175 1180

Gly Ile Arg His Asp Ala Gly Asp Ile Gly Tyr Leu Lys Gly Leu Phe
1185 1190 1195 1200

Ser Tyr Gly Arg Tyr Lys Asn Ser Ile Ser Arg Ser Thr Gly Ala Asp
1205 1210 1215

Glu His Ala Glu Gly Ser Val Asn Gly Thr Leu Met Gln Leu Gly Ala
1220 1225 1230

Leu Gly Gly Val Asn Val Pro Phe Ala Ala Thr Gly Asp Leu Thr Val
1235 1240 1245

Glu Gly Gly Leu Arg Tyr Asp Leu Leu Lys Gln Asp Ala Phe Ala Glu
1250 1255 1260

Lys Gly Ser Ala Leu Gly Trp Ser Gly Asn Ser Leu Thr Glu Gly Thr
1265 1270 1275 1280

Leu Val Gly Leu Ala Gly Leu Lys Leu Ser Gln Pro Leu Ser Asp Lys
1285 1290 1295

Ala Val Leu Phe Ala Thr Ala Gly Val Glu Arg Asp Leu Asn Gly Arg
1300 1305 1310

Asp Tyr Thr Val Thr Gly Gly Phe Thr Gly Ala Thr Ala Ala Thr Gly
1315 1320 1325

Lys Thr Gly Ala Arg Asn Met Pro His Thr Arg Leu Val Ala Gly Leu
1330 1335 1340

Gly Ala Asp Val Glu Phe Gly Asn Gly Trp Asn Gly Leu Ala Arg Tyr
1345 1350 1355 1360

Ser Tyr Ala Gly Ser Lys Gln Tyr Gly Asn His Ser Gly Arg Val Gly
1365 1370 1375

Val Gly Tyr Arg Phe Leu Glu His His His His His His
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<212> DNA
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<223> 961cL-ORF46.1

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gcattcaacg atatcgccga ttcattggat gaaaccaaca ctaaggcaga cgaagccgtc 600
aaaaccgcca atgaagccaa acagacggcc gaagaaacca aacaaaacgt cgatgccaaa 660

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cgcttggctt ctgctgaaaa atccattgcc gatcacgata ctcgcctgaa cggtttggat    960
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aacgattctt ttatccggca ggttctcgac cgtcagcatt tcgaacccga cgggaaatac   1140
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cgccacccga agacaggcgt accgtttgac ggtaaagggt ttccgaattt tgagaagcac   2280
gtgaaatatg atacgtaact cgag                                          2304
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<210> 159
<211> 765
<212> PRT
<213> Artificial Sequence

<220>
<223> 961cL-ORF46.1

<400> 159

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            20                  25                  30

Ala Ala Thr Val Ala Ile Ala Ala Ala Tyr Asn Asn Gly Gln Glu Ile
        35                  40                  45

Asn Gly Phe Lys Ala Gly Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly
    50                  55                  60

Thr Ile Thr Lys Lys Asp Ala Thr Ala Ala Asp Val Glu Ala Asp Asp
65                  70                  75                  80

Phe Lys Gly Leu Gly Leu Lys Lys Val Val Thr Asn Leu Thr Lys Thr
                85                  90                  95

Val Asn Glu Asn Lys Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu
            100                 105                 110

Ser Glu Ile Glu Lys Leu Thr Thr Lys Leu Ala Asp Thr Asp Ala Ala
        115                 120                 125

Leu Ala Asp Thr Asp Ala Ala Leu Asp Ala Thr Thr Asn Ala Leu Asn
    130                 135                 140

Lys Leu Gly Glu Asn Ile Thr Thr Phe Ala Glu Glu Thr Lys Thr Asn
145                 150                 155                 160

Ile Val Lys Ile Asp Glu Lys Leu Glu Ala Val Ala Asp Thr Val Asp
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165 170 175

Lys His Ala Glu Ala Phe Asn Asp Ile Ala Asp Ser Leu Asp Glu Thr
180 185 190

Asn Thr Lys Ala Asp Glu Ala Val Lys Thr Ala Asn Glu Ala Lys Gln
195 200 205

Thr Ala Glu Glu Thr Lys Gln Asn Val Asp Ala Lys Val Lys Ala Ala
210 215 220

Glu Thr Ala Ala Gly Lys Ala Glu Ala Ala Ala Gly Thr Ala Asn Thr
225 230 235 240

Ala Ala Asp Lys Ala Glu Ala Val Ala Ala Lys Val Thr Asp Ile Lys
245 250 255

Ala Asp Ile Ala Thr Asn Lys Asp Asn Ile Ala Lys Lys Ala Asn Ser
260 265 270

Ala Asp Val Tyr Thr Arg Glu Glu Ser Asp Ser Lys Phe Val Arg Ile
275 280 285

Asp Gly Leu Asn Ala Thr Thr Glu Lys Leu Asp Thr Arg Leu Ala Ser
290 295 300

Ala Glu Lys Ser Ile Ala Asp His Asp Thr Arg Leu Asn Gly Leu Asp
305 310 315 320

Lys Thr Val Ser Asp Leu Arg Lys Glu Thr Arg Gln Gly Leu Ala Glu
325 330 335

Gln Ala Ala Leu Ser Gly Leu Phe Gln Pro Tyr Asn Val Gly Gly Ser
340 345 350

Gly Gly Gly Gly Ser Asp Leu Ala Asn Asp Ser Phe Ile Arg Gln Val
355 360 365

Leu Asp Arg Gln His Phe Glu Pro Asp Gly Lys Tyr His Leu Phe Gly
370 375 380

Ser Arg Gly Glu Leu Ala Glu Arg Ser Gly His Ile Gly Leu Gly Lys
385 390 395 400

Ile Gln Ser His Gln Leu Gly Asn Leu Met Ile Gln Gln Ala Ala Ile
405 410 415

Lys Gly Asn Ile Gly Tyr Ile Val Arg Phe Ser Asp His Gly His Glu
420 425 430

Val His Ser Pro Phe Asp Asn His Ala Ser His Ser Asp Ser Asp Glu
435 440 445

Ala Gly Ser Pro Val Asp Gly Phe Ser Leu Tyr Arg Ile His Trp Asp
450 455 460

Gly Tyr Glu His His Pro Ala Asp Gly Tyr Asp Gly Pro Gln Gly Gly
465 470 475 480

Gly Tyr Pro Ala Pro Lys Gly Ala Arg Asp Ile Tyr Ser Tyr Asp Ile
485 490 495

Lys Gly Val Ala Gln Asn Ile Arg Leu Asn Leu Thr Asp Asn Arg Ser
500 505 510

Thr Gly Gln Arg Leu Ala Asp Arg Phe His Asn Ala Gly Ser Met Leu
515 520 525

Thr Gln Gly Val Gly Asp Gly Phe Lys Arg Ala Thr Arg Tyr Ser Pro

530 535 540

Glu Leu Asp Arg Ser Gly Asn Ala Ala Glu Ala Phe Asn Gly Thr Ala
545 550 555 560

Asp Ile Val Lys Asn Ile Ile Gly Ala Ala Gly Glu Ile Val Gly Ala
565 570 575

Gly Asp Ala Val Gln Gly Ile Ser Glu Gly Ser Asn Ile Ala Val Met
580 585 590

His Gly Leu Gly Leu Leu Ser Thr Glu Asn Lys Met Ala Arg Ile Asn
595 600 605

Asp Leu Ala Asp Met Ala Gln Leu Lys Asp Tyr Ala Ala Ala Ala Ile
610 615 620

Arg Asp Trp Ala Val Gln Asn Pro Asn Ala Ala Gln Gly Ile Glu Ala
625 630 635 640

Val Ser Asn Ile Phe Met Ala Ala Ile Pro Ile Lys Gly Ile Gly Ala
645 650 655

Val Arg Gly Lys Tyr Gly Leu Gly Gly Ile Thr Ala His Pro Ile Lys
660 665 670

Arg Ser Gln Met Gly Ala Ile Ala Leu Pro Lys Gly Lys Ser Ala Val
675 680 685

Ser Asp Asn Phe Ala Asp Ala Ala Tyr Ala Lys Tyr Pro Ser Pro Tyr
690 695 700

His Ser Arg Asn Ile Arg Ser Asn Leu Glu Gln Arg Tyr Gly Lys Glu
705 710 715 720

Asn Ile Thr Ser Ser Thr Val Pro Pro Ser Asn Gly Lys Asn Val Lys
725 730 735

Leu Ala Asp Gln Arg His Pro Lys Thr Gly Val Pro Phe Asp Gly Lys
740 745 750

Gly Phe Pro Asn Phe Glu Lys His Val Lys Tyr Asp Thr
755 760 765

<210> 160
<211> 1839
<212> DNA
<213> Artificial Sequence

<220>
<223> 961cL-741

<400> 160
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gcctacaaca atggccaaga aatcaacggt ttcaaagctg gagagaccat ctacgacatt 180
gatgaagacg gcacaattac caaaaaagac gcaactgcag ccgatgttga agccgacgac 240
tttaaaggtc tgggtctgaa aaaagtcgtg actaacctga ccaaaaccgt caatgaaaac 300
aaacaaaacg tcgatgccaa agtaaaagct gcagaatctg aaatagaaaa gttaacaacc 360
aagttagcag acactgatgc cgctttagca gatactgatg ccgctctgga tgcaaccacc 420
aacgccttga ataaattggg agaaaatata acgacatttg ctgaagagac taagacaaat 480
atcgtaaaaa ttgatgaaaa attagaagcc gtggctgata ccgtcgacaa gcatgccgaa 540
gcattcaacg atatcgccga ttcattggat gaaaccaaca ctaaggcaga cgaagccgtc 600
aaaaccgcca atgaagccaa acagacggcc gaagaaacca aacaaaacgt cgatgccaaa 660
gtaaaagctg cagaaactgc agcaggcaaa gccgaagctg ccgctggcac agctaatact 720
gcagccgaca aggccgaagc tgtcgctgca aaagttaccg acatcaaagc tgatatcgct 780
acgaacaaag ataatattgc taaaaaagca aacagtgccg acgtgtacac cagagaagag 840
tctgacagca aatttgtcag aattgatggt ctgaacgcta ctaccgaaaa attggacaca 900
cgcttggctt ctgctgaaaa atccattgcc gatcacgata ctcgcctgaa cggtttggat 960

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atcggtgcgg ggcttgccga tgcactaacc gcaccgctcg accataaaga caaaggtttg    1140
cagtctttga cgctggatca gtccgtcagg aaaaacgaga aactgaagct ggcggcacaa    1200
ggtgcggaaa aaacttatgg aaacggtgac agcctcaata cgggcaaatt gaagaacgac    1260
aaggtcagcc gtttcgactt tatccgccaa atcgaagtgg acgggcagct cattaccttg    1320
gagagtggag agttccaagt atacaaacaa agccattccg ccttaaccgc ctttcagacc    1380
gagcaaatac aagattcgga gcattccggg aagatggttg cgaaacgcca gttcagaatc    1440
ggcgacatag cgggcgaaca tacatctttt gacaagcttc ccgaaggcgg cagggcgaca    1500
tatcgcggga cggcgttcgg ttcagacgat gccggcggaa aactgaccta caccatagat    1560
ttcgccgcca agcagggaaa cggcaaaatc gaacatttga aatcgccaga actcaatgtc    1620
gacctggccg ccgccgatat caagccggat ggaaaacgcc atgccgtcat cagcggttcc    1680
gtcctttaca accaagccga gaaaggcagt tactccctcg gtatctttgg cggaaaagcc    1740
caggaagttg ccggcagcgc ggaagtgaaa accgtaaacg gcatacgcca tatcggcctt    1800
gccgccaagc aactcgagca ccaccaccac caccactga                           1839
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<210> 161
<211> 612
<212> PRT
<213> Artificial Sequence

<220>
<223> 961cL-741

<400> 161

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Met Lys His Phe Pro Ser Lys Val Leu Thr Thr Ala Ile Leu Ala Thr
1               5                   10                  15

Phe Cys Ser Gly Ala Leu Ala Ala Thr Asn Asp Asp Asp Val Lys Lys
            20                  25                  30

Ala Ala Thr Val Ala Ile Ala Ala Ala Tyr Asn Asn Gly Gln Glu Ile
        35                  40                  45

Asn Gly Phe Lys Ala Gly Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly
    50                  55                  60

Thr Ile Thr Lys Lys Asp Ala Thr Ala Ala Asp Val Glu Ala Asp Asp
65                  70                  75                  80

Phe Lys Gly Leu Gly Leu Lys Lys Val Val Thr Asn Leu Thr Lys Thr
                85                  90                  95

Val Asn Glu Asn Lys Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu
            100                 105                 110

Ser Glu Ile Glu Lys Leu Thr Thr Lys Leu Ala Asp Thr Asp Ala Ala
        115                 120                 125

Leu Ala Asp Thr Asp Ala Ala Leu Asp Ala Thr Thr Asn Ala Leu Asn
    130                 135                 140

Lys Leu Gly Glu Asn Ile Thr Thr Phe Ala Glu Glu Thr Lys Thr Asn
145                 150                 155                 160

Ile Val Lys Ile Asp Glu Lys Leu Glu Ala Val Ala Asp Thr Val Asp
                165                 170                 175

Lys His Ala Glu Ala Phe Asn Asp Ile Ala Asp Ser Leu Asp Glu Thr
            180                 185                 190

Asn Thr Lys Ala Asp Glu Ala Val Lys Thr Ala Asn Glu Ala Lys Gln
        195                 200                 205

Thr Ala Glu Glu Thr Lys Gln Asn Val Asp Ala Lys Val Lys Ala Ala
    210                 215                 220

Glu Thr Ala Ala Gly Lys Ala Glu Ala Ala Ala Gly Thr Ala Asn Thr
225                 230                 235                 240
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Ala Ala Asp Lys Ala Glu Ala Val Ala Ala Lys Val Thr Asp Ile Lys
                245                 250                 255

Ala Asp Ile Ala Thr Asn Lys Asp Asn Ile Ala Lys Lys Ala Asn Ser
            260                 265                 270

Ala Asp Val Tyr Thr Arg Glu Glu Ser Asp Ser Lys Phe Val Arg Ile
        275                 280                 285

Asp Gly Leu Asn Ala Thr Thr Glu Lys Leu Asp Thr Arg Leu Ala Ser
    290                 295                 300

Ala Glu Lys Ser Ile Ala Asp His Asp Thr Arg Leu Asn Gly Leu Asp
305                 310                 315                 320

Lys Thr Val Ser Asp Leu Arg Lys Glu Thr Arg Gln Gly Leu Ala Glu
                325                 330                 335

Gln Ala Ala Leu Ser Gly Leu Phe Gln Pro Tyr Asn Val Gly Gly Ser
            340                 345                 350

Gly Gly Gly Gly Val Ala Ala Asp Ile Gly Ala Gly Leu Ala Asp Ala
        355                 360                 365

Leu Thr Ala Pro Leu Asp His Lys Asp Lys Gly Leu Gln Ser Leu Thr
    370                 375                 380

Leu Asp Gln Ser Val Arg Lys Asn Glu Lys Leu Lys Leu Ala Ala Gln
385                 390                 395                 400

Gly Ala Glu Lys Thr Tyr Gly Asn Gly Asp Ser Leu Asn Thr Gly Lys
                405                 410                 415

Leu Lys Asn Asp Lys Val Ser Arg Phe Asp Phe Ile Arg Gln Ile Glu
            420                 425                 430

Val Asp Gly Gln Leu Ile Thr Leu Glu Ser Gly Glu Phe Gln Val Tyr
        435                 440                 445

Lys Gln Ser His Ser Ala Leu Thr Ala Phe Gln Thr Glu Gln Ile Gln
    450                 455                 460

Asp Ser Glu His Ser Gly Lys Met Val Ala Lys Arg Gln Phe Arg Ile
465                 470                 475                 480

Gly Asp Ile Ala Gly Glu His Thr Ser Phe Asp Lys Leu Pro Glu Gly
                485                 490                 495

Gly Arg Ala Thr Tyr Arg Gly Thr Ala Phe Gly Ser Asp Asp Ala Gly
            500                 505                 510

Gly Lys Leu Thr Tyr Thr Ile Asp Phe Ala Ala Lys Gln Gly Asn Gly
        515                 520                 525

Lys Ile Glu His Leu Lys Ser Pro Glu Leu Asn Val Asp Leu Ala Ala
    530                 535                 540

Ala Asp Ile Lys Pro Asp Gly Lys Arg His Ala Val Ile Ser Gly Ser
545                 550                 555                 560

Val Leu Tyr Asn Gln Ala Glu Lys Gly Ser Tyr Ser Leu Gly Ile Phe
                565                 570                 575

Gly Gly Lys Ala Gln Glu Val Ala Gly Ser Ala Glu Val Lys Thr Val
            580                 585                 590

Asn Gly Ile Arg His Ile Gly Leu Ala Ala Lys Gln Leu Glu His His
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His His His His
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<210> 162
<211> 4218
<212> DNA
<213> Artificial Sequence

<220>
<223> 961cL-983

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gcctacaaca atggccaaga aatcaacggt ttcaaagctg gagagaccat ctacgacatt 180
gatgaagacg gcacaattac caaaaaagac gcaactgcag ccgatgttga agccgacgac 240
tttaaaggtc tgggtctgaa aaaagtcgtg actaacctga ccaaaaccgt caatgaaaac 300
aaacaaaacg tcgatgccaa agtaaaagct gcagaatctg aaatagaaaa gttaacaacc 360
aagttagcag acactgatgc cgctttagca gatactgatg ccgctctgga tgcaaccacc 420
aacgccttga ataaattggg agaaaatata acgacatttg ctgaagagac taagacaaat 480
atcgtaaaaa ttgatgaaaa attagaagcc gtggctgata ccgtcgacaa gcatgccgaa 540
gcattcaacg atatcgccga ttcattggat gaaaccaaca ctaaggcaga cgaagccgtc 600
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gtaaaagctg cagaaactgc agcaggcaaa gccgaagctg ccgctggcac agctaatact 720
gcagccgaca aggccgaagc tgtcgctgca aaagttaccg acatcaaagc tgatatcgct 780
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ttcaacagtc tcgccgctac cgtctatgcc gacagtaccg ccgcccatgc cgatatgcag 3360

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ggacgccgcc tgaaagccgt atcggacggg ttggaccaca acggcacggg tctgcgcgtc    3420
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cgcggcagta cccaaaccgt cggcattgcc gcgaaaaccg gcgaaaatac gacagcagcc    3540
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cgtctggttg ccggcctggg cgcggatgtc gaattcggca acggctggaa cggcttggca    4140
cgttacagct acgccggttc caaacagtac ggcaaccaca gcggacgagt cggcgtaggc    4200
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<210> 163
<211> 1403
<212> PRT
<213> Artificial Sequence

<220>
<223> 961cL-983

<400> 163

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Phe Cys Ser Gly Ala Leu Ala Ala Thr Asn Asp Asp Asp Val Lys Lys
            20                  25                  30

Ala Ala Thr Val Ala Ile Ala Ala Ala Tyr Asn Asn Gly Gln Glu Ile
        35                  40                  45

Asn Gly Phe Lys Ala Gly Glu Thr Ile Tyr Asp Ile Asp Glu Asp Gly
    50                  55                  60

Thr Ile Thr Lys Lys Asp Ala Thr Ala Ala Asp Val Glu Ala Asp Asp
65                  70                  75                  80

Phe Lys Gly Leu Gly Leu Lys Lys Val Val Thr Asn Leu Thr Lys Thr
                85                  90                  95

Val Asn Glu Asn Lys Gln Asn Val Asp Ala Lys Val Lys Ala Ala Glu
            100                 105                 110

Ser Glu Ile Glu Lys Leu Thr Thr Lys Leu Ala Asp Thr Asp Ala Ala
        115                 120                 125

Leu Ala Asp Thr Asp Ala Ala Leu Asp Ala Thr Thr Asn Ala Leu Asn
    130                 135                 140

Lys Leu Gly Glu Asn Ile Thr Thr Phe Ala Glu Glu Thr Lys Thr Asn
145                 150                 155                 160

Ile Val Lys Ile Asp Glu Lys Leu Glu Ala Val Ala Asp Thr Val Asp
                165                 170                 175

Lys His Ala Glu Ala Phe Asn Asp Ile Ala Asp Ser Leu Asp Glu Thr
            180                 185                 190

Asn Thr Lys Ala Asp Glu Ala Val Lys Thr Ala Asn Glu Ala Lys Gln
        195                 200                 205

Thr Ala Glu Glu Thr Lys Gln Asn Val Asp Ala Lys Val Lys Ala Ala
    210                 215                 220

Glu Thr Ala Ala Gly Lys Ala Glu Ala Ala Ala Gly Thr Ala Asn Thr
225                 230                 235                 240
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Ala Ala Asp Lys Ala Glu Ala Val Ala Ala Lys Val Thr Asp Ile Lys
                245                 250                 255

Ala Asp Ile Ala Thr Asn Lys Asp Asn Ile Ala Lys Lys Ala Asn Ser
            260                 265                 270

Ala Asp Val Tyr Thr Arg Glu Glu Ser Asp Ser Lys Phe Val Arg Ile
        275                 280                 285

Asp Gly Leu Asn Ala Thr Thr Glu Lys Leu Asp Thr Arg Leu Ala Ser
    290                 295                 300

Ala Glu Lys Ser Ile Ala Asp His Asp Thr Arg Leu Asn Gly Leu Asp
305                 310                 315                 320

Lys Thr Val Ser Asp Leu Arg Lys Glu Thr Arg Gln Gly Leu Ala Glu
                325                 330                 335

Gln Ala Ala Leu Ser Gly Leu Phe Gln Pro Tyr Asn Val Gly Gly Ser
            340                 345                 350

Gly Gly Gly Gly Thr Ser Ala Pro Asp Phe Asn Ala Gly Gly Thr Gly
        355                 360                 365

Ile Gly Ser Asn Ser Arg Ala Thr Thr Ala Lys Ser Ala Ala Val Ser
    370                 375                 380

Tyr Ala Gly Ile Lys Asn Glu Met Cys Lys Asp Arg Ser Met Leu Cys
385                 390                 395                 400

Ala Gly Arg Asp Asp Val Ala Val Thr Asp Arg Asp Ala Lys Ile Asn
                405                 410                 415

Ala Pro Pro Pro Asn Leu His Thr Gly Asp Phe Pro Asn Pro Asn Asp
            420                 425                 430

Ala Tyr Lys Asn Leu Ile Asn Leu Lys Pro Ala Ile Glu Ala Gly Tyr
        435                 440                 445

Thr Gly Arg Gly Val Glu Val Gly Ile Val Asp Thr Gly Glu Ser Val
    450                 455                 460

Gly Ser Ile Ser Phe Pro Glu Leu Tyr Gly Arg Lys Glu His Gly Tyr
465                 470                 475                 480

Asn Glu Asn Tyr Lys Asn Tyr Thr Ala Tyr Met Arg Lys Glu Ala Pro
                485                 490                 495

Glu Asp Gly Gly Gly Lys Asp Ile Glu Ala Ser Phe Asp Asp Glu Ala
            500                 505                 510

Val Ile Glu Thr Glu Ala Lys Pro Thr Asp Ile Arg His Val Lys Glu
        515                 520                 525

Ile Gly His Ile Asp Leu Val Ser His Ile Ile Gly Gly Arg Ser Val
    530                 535                 540

Asp Gly Arg Pro Ala Gly Gly Ile Ala Pro Asp Ala Thr Leu His Ile
545                 550                 555                 560

Met Asn Thr Asn Asp Glu Thr Lys Asn Glu Met Met Val Ala Ala Ile
                565                 570                 575

Arg Asn Ala Trp Val Lys Leu Gly Glu Arg Gly Val Arg Ile Val Asn
            580                 585                 590

Asn Ser Phe Gly Thr Thr Ser Arg Ala Gly Thr Ala Asp Leu Phe Gln
        595                 600                 605
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Ile Ala Asn Ser Glu Glu Gln Tyr Arg Gln Ala Leu Leu Asp Tyr Ser
610 615 620

Gly Gly Asp Lys Thr Asp Glu Gly Ile Arg Leu Met Gln Gln Ser Asp
625 630 635 640

Tyr Gly Asn Leu Ser Tyr His Ile Arg Asn Lys Asn Met Leu Phe Ile
645 650 655

Phe Ser Thr Gly Asn Asp Ala Gln Ala Gln Pro Asn Thr Tyr Ala Leu
660 665 670

Leu Pro Phe Tyr Glu Lys Asp Ala Gln Lys Gly Ile Ile Thr Val Ala
675 680 685

Gly Val Asp Arg Ser Gly Glu Lys Phe Lys Arg Glu Met Tyr Gly Glu
690 695 700

Pro Gly Thr Glu Pro Leu Glu Tyr Gly Ser Asn His Cys Gly Ile Thr
705 710 715 720

Ala Met Trp Cys Leu Ser Ala Pro Tyr Glu Ala Ser Val Arg Phe Thr
725 730 735

Arg Thr Asn Pro Ile Gln Ile Ala Gly Thr Ser Phe Ser Ala Pro Ile
740 745 750

Val Thr Gly Thr Ala Ala Leu Leu Leu Gln Lys Tyr Pro Trp Met Ser
755 760 765

Asn Asp Asn Leu Arg Thr Thr Leu Leu Thr Thr Ala Gln Asp Ile Gly
770 775 780

Ala Val Gly Val Asp Ser Lys Phe Gly Trp Gly Leu Leu Asp Ala Gly
785 790 795 800

Lys Ala Met Asn Gly Pro Ala Ser Phe Pro Phe Gly Asp Phe Thr Ala
805 810 815

Asp Thr Lys Gly Thr Ser Asp Ile Ala Tyr Ser Phe Arg Asn Asp Ile
820 825 830

Ser Gly Thr Gly Gly Leu Ile Lys Lys Gly Gly Ser Gln Leu Gln Leu
835 840 845

His Gly Asn Asn Thr Tyr Thr Gly Lys Thr Ile Ile Glu Gly Gly Ser
850 855 860

Leu Val Leu Tyr Gly Asn Asn Lys Ser Asp Met Arg Val Glu Thr Lys
865 870 875 880

Gly Ala Leu Ile Tyr Asn Gly Ala Ala Ser Gly Gly Ser Leu Asn Ser
885 890 895

Asp Gly Ile Val Tyr Leu Ala Asp Thr Asp Gln Ser Gly Ala Asn Glu
900 905 910

Thr Val His Ile Lys Gly Ser Leu Gln Leu Asp Gly Lys Gly Thr Leu
915 920 925

Tyr Thr Arg Leu Gly Lys Leu Leu Lys Val Asp Gly Thr Ala Ile Ile
930 935 940

Gly Gly Lys Leu Tyr Met Ser Ala Arg Gly Lys Gly Ala Gly Tyr Leu
945 950 955 960

Asn Ser Thr Gly Arg Arg Val Pro Phe Leu Ser Ala Ala Lys Ile Gly
965 970 975

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Gln Asp Tyr Ser Phe Phe Thr Asn Ile Glu Thr Asp Gly Gly Leu Leu
            980                 985                 990

Ala Ser Leu Asp Ser Val Glu Lys Thr Ala Gly Ser Glu Gly Asp Thr
        995                 1000                1005

Leu Ser Tyr Tyr Val Arg Arg Gly Asn Ala Ala Arg Thr Ala Ser Ala
    1010                1015                1020

Ala Ala His Ser Ala Pro Ala Gly Leu Lys His Ala Val Glu Gln Gly
1025                1030                1035                1040

Gly Ser Asn Leu Glu Asn Leu Met Val Glu Leu Asp Ala Ser Glu Ser
                1045                1050                1055

Ser Ala Thr Pro Glu Thr Val Glu Thr Ala Ala Ala Asp Arg Thr Asp
            1060                1065                1070

Met Pro Gly Ile Arg Pro Tyr Gly Ala Thr Phe Arg Ala Ala Ala Ala
        1075                1080                1085

Val Gln His Ala Asn Ala Ala Asp Gly Val Arg Ile Phe Asn Ser Leu
    1090                1095                1100

Ala Ala Thr Val Tyr Ala Asp Ser Thr Ala Ala His Ala Asp Met Gln
1105                1110                1115                1120

Gly Arg Arg Leu Lys Ala Val Ser Asp Gly Leu Asp His Asn Gly Thr
                1125                1130                1135

Gly Leu Arg Val Ile Ala Gln Thr Gln Gln Asp Gly Gly Thr Trp Glu
            1140                1145                1150

Gln Gly Gly Val Glu Gly Lys Met Arg Gly Ser Thr Gln Thr Val Gly
        1155                1160                1165

Ile Ala Ala Lys Thr Gly Glu Asn Thr Thr Ala Ala Ala Thr Leu Gly
    1170                1175                1180

Met Gly Arg Ser Thr Trp Ser Glu Asn Ser Ala Asn Ala Lys Thr Asp
1185                1190                1195                1200

Ser Ile Ser Leu Phe Ala Gly Ile Arg His Asp Ala Gly Asp Ile Gly
                1205                1210                1215

Tyr Leu Lys Gly Leu Phe Ser Tyr Gly Arg Tyr Lys Asn Ser Ile Ser
            1220                1225                1230

Arg Ser Thr Gly Ala Asp Glu His Ala Glu Gly Ser Val Asn Gly Thr
        1235                1240                1245

Leu Met Gln Leu Gly Ala Leu Gly Gly Val Asn Val Pro Phe Ala Ala
    1250                1255                1260

Thr Gly Asp Leu Thr Val Glu Gly Gly Leu Arg Tyr Asp Leu Leu Lys
1265                1270                1275                1280

Gln Asp Ala Phe Ala Glu Lys Gly Ser Ala Leu Gly Trp Ser Gly Asn
                1285                1290                1295

Ser Leu Thr Glu Gly Thr Leu Val Gly Leu Ala Gly Leu Lys Leu Ser
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Gln Pro Leu Ser Asp Lys Ala Val Leu Phe Ala Thr Ala Gly Val Glu
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Arg Asp Leu Asn Gly Arg Asp Tyr Thr Val Thr Gly Gly Phe Thr Gly
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Ser Ala Gln Gly Ser Gln Asp Met Ala Ala Val Ser Glu Glu Asn Thr
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Val Ala Gln Asn Asp Met Pro Gln Asn Ala Ala Gly Thr Asp Ser Ser
            100   105   110

Thr Pro Asn His Thr Pro Asp Pro Asn Met Leu Ala Gly Asn Met Glu
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Asn Gln Ala Thr Asp Ala Gly Glu Ser Ser Gln Pro Ala Asn Gln Pro
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Asp Met Ala Asn Ala Ala Asp Gly Met Gln Gly Asp Asp Pro Ser Ala
145   150   155   160

Gly Gly Gln Asn Ala Gly Asn Thr Ala Ala Gln Gly Ala Asn Gln Ala
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Gly Asn Asn Gln Ala Ala Gly Ser Ser Asp Pro Ile Pro Ala Ser Asn
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Pro Ala Pro Ala Asn Gly Gly Ser Asn Phe Gly Arg Val Asp Leu Ala
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Asn Gly Val Leu Ile Asp Gly Pro Ser Gln Asn Ile Thr Leu Thr His
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Cys Lys Gly Asp Ser Cys Ser Gly Asn Asn Phe Leu Asp Glu Glu Val
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Gln Leu Lys Ser Glu Phe Glu Lys Leu Ser Asp Ala Asp Lys Ile Ser
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Asp Ser Val Gln Met Lys Gly Ile Asn Gln Tyr Ile Ile Phe Tyr Lys
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Pro Lys Pro Thr Ser Phe Ala Arg Phe Arg Arg Ser Ala Arg Ser Arg
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305   310   315   320

Thr Leu Ile Val Asp Gly Glu Ala Val Ser Leu Thr Gly His Ser Gly
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Ala Lys Gly Glu Met Leu Ala Gly Ala Ala Val Tyr Asn Gly Glu Val
370 375 380

Leu His Phe His Thr Glu Asn Gly Arg Pro Tyr Pro Thr Arg Gly Arg
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Phe Ala Ala Lys Val Asp Phe Gly Ser Lys Ser Val Asp Gly Ile Ile
405 410 415

Asp Ser Gly Asp Asp Leu His Met Gly Thr Gln Lys Phe Lys Ala Ala
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Ile Asp Gly Asn Gly Phe Lys Gly Thr Trp Thr Glu Asn Gly Ser Gly
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Asp Val Ser Gly Lys Phe Tyr Gly Pro Ala Gly Glu Glu Val Ala Gly
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35 40 45

Val Lys Glu Asp Ala Pro Gln Ala Gly Ser Gln Gly Gln Gly Ala Pro
50 55 60

Ser Thr Gln Gly Ser Gln Asp Met Ala Ala Val Ser Ala Glu Asn Thr
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Gly Asn Gly Gly Ala Ala Thr Thr Asp Lys Pro Lys Asn Glu Asp Glu
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Gly Pro Gln Asn Asp Met Pro Gln Asn Ser Ala Glu Ser Ala Asn Gln
100 105 110

Thr Gly Asn Asn Gln Pro Ala Asp Ser Ser Asp Ser Ala Pro Ala Ser
115 120 125

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130 135 140

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145 150 155 160

His Cys Lys Gly Asp Ser Cys Asn Gly Asp Asn Leu Leu Asp Glu Glu
165 170 175

Ala Pro Ser Lys Ser Glu Phe Glu Asn Leu Asn Glu Ser Glu Arg Ile
180 185 190

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Ala Thr Ala Val Gln Ala Asn Gly Thr Asn Lys Tyr Val Ile Ile Tyr
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Arg Ser Arg Arg Ser Leu Pro Ala Glu Met Pro Leu Ile Pro Val Asn
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Gln Ala Asp Thr Leu Ile Val Asp Gly Glu Ala Val Ser Leu Thr Gly
            260                 265                 270

His Ser Gly Asn Ile Phe Ala Pro Glu Gly Asn Tyr Arg Tyr Leu Thr
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Tyr Gly Ala Glu Lys Leu Pro Gly Gly Ser Tyr Ala Leu Arg Val Gln
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Gly Glu Pro Ala Lys Gly Glu Met Leu Ala Gly Thr Ala Val Tyr Asn
305                 310                 315                 320

Gly Glu Val Leu His Phe His Thr Glu Asn Gly Arg Pro Tyr Pro Thr
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Arg Gly Arg Phe Ala Ala Lys Val Asp Phe Gly Ser Lys Ser Val Asp
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Gly Ile Ile Asp Ser Gly Asp Asp Leu His Met Gly Thr Gln Lys Phe
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Lys Ala Ala Ile Asp Gly Asn Gly Phe Lys Gly Thr Trp Thr Glu Asn
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Gly Gly Gly Asp Val Ser Gly Arg Phe Tyr Gly Pro Ala Gly Glu Glu
385                 390                 395                 400

Val Ala Gly Lys Tyr Ser Tyr Arg Pro Thr Asp Ala Glu Lys Gly Gly
                405                 410                 415

Phe Gly Val Phe Ala Gly Lys Lys Glu Gln Asp
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```

Claims

1. A method for the heterologous expression of a protein of the invention, in which (a) at least one domain in the protein is deleted and, optionally, (b) no fusion partner is used.

2. The method of claim 1, in which the protein of the invention is ORF46.

3. The method of claim 2, in which ORF46 is divided into a first domain (amino acids 1-433) and a second domain (amino acids 433-608).

4. The method of claim 2, in which the protein of the invention is 564.

5. The method of claim 4, in which protein 564 is divided into domains as shown in Figure 8.

6. The method of claim 1 in which the protein of the invention is 961.

7. The method of claim 6, in which protein 961 is divided into domains as shown in Figure 12.

8. The method of claim 1, in which the protein of the invention is 502 and the domain is amino acids 28 to 167 (numbered according to the MC58 sequence).

9. The method of claim 1, in which the protein of the invention is 287.

10. A method for the heterologous expression of a protein of the invention, in which (a) a portion of the N-terminal domain of the protein is deleted.

11. The method of claim 9 or claim 10, in which protein 287 is divided into domains A B & C shown in Figure 5.

12. The method of claim 11, in which (i) domain A, (ii) domains A and B, or (iii) domains A and C are deleted.

13. The method of claim 11, wherein (i) amino acids 1-17, (ii) amino acids 1-25, (iii) amino acids 1-69, or (iv) amino acids 1-106, of domain A are deleted.

14. A method for the heterologous expression of a protein of the invention, in which (a) no fusion partner is used, and (b) the protein's native leader peptide (if present) is used.

15. The method of claim 14, in which the protein of the invention is selected from the group consisting of: 111, 149, 206, 225-1, 235, 247-1, 274, 283, 286, 292, 401, 406, 502-1, 503, 519-1, 525-1, 552, 556, 557, 570, 576-1, 580, 583, 664, 759, 907, 913, 920-1, 936-1, 953, 961, 983, 989, Orf4, Orf7-1, Orf9-1, Orf23, Orf25, Orf37, Orf38, Orf40, Orf40.1, Orf40.2, Orf72-1, Orf76-1, Orf85-2, Orf91, Orf97-1, Orf119, Orf143.1, NMB0109, NMB2050, 008, 105, 117-1, 121-1, 122-1, 128-1, 148, 216, 243, 308, 593, 652, 726, 926, 982, Orf83-1 and Orf143-1.

16. A method for the heterologous expression of a protein of the invention, in which (a) the protein's leader peptide is replaced by the leader peptide from a different protein and, optionally, (b) no fusion partner is used.

17. The method of claim 16, in which the different protein is 961, ORF4, *E.coli* OmpA, or *E.carotovora* PelB, or in which the leader peptide is MKKYLFSAA.

18. The method of claim 17, in which the different protein is *E.coli* OmpA and the protein of the invention is ORF1.

19. The method of claim 17, in which the protein of the invention is 911 and the different protein is *E.carotovora* PelB or *E.coli* OmpA.

20. The method of claim 17, in which the different protein is ORF4 and the protein of the invention is 287.

21. A method for the heterologous expression of a protein of the invention, in which (a) the protein's leader peptide is deleted and, optionally, (b) no fusion partner is used.

22. The method of claim 21, in which the protein of the invention is 919.

23. A method for the heterologous expression of a protein of the invention, in which expression of a protein of the invention is carried out at a temperature at which a toxic activity of the protein is not manifested.

24. The method of claim 23, in which protein 919 is expressed at 30°C.

25. A method for the heterologous expression of a protein of the invention, in which protein is mutated to reduce or eliminate toxic activity.

26. The method of claim 25, in which the protein of the invention is 907, 919 or 922.

27. The method of claim 26, in which 907 is mutated at Glu-117 (*e.g.* Glu→Gly).

28. The method of claim 26, in which 919 is mutated at Glu-255 (*e.g.* Glu→Gly) and/or Glu-323 (*e.g.* Glu→Gly).

29. The method of claim 26, in which 922 is mutated at Glu-164 (*e.g.* Glu→Gly), Ser-213 (*e.g.* Ser→Gly) and/or Asn-348 (*e.g.* Asn→Gly).

30. A method for the heterologous expression of a protein of the invention, in which vector pSM214 is used or vector pET-24b is used.

31. The method of claim 30, in which the protein of the invention is 953 and the vector is pSM214.

32. A method for the heterologous expression of a protein of the invention, in which a protein is expressed or purified such that it adopts a particular multimeric form.

33. The method of claim 32, in which protein 953 is expressed and/or purified in monomeric form.

34. The method of claim 32, in which protein 961 is expressed and/or purified in tetrameric form.

35. The method of claim 32, in which protein 287 is expressed and/or purified in dimeric form.

36. The method of claim 32, in which protein 919 is expressed and/or purified in monomeric form.

37. A method for the heterologous expression of a protein of the invention, in which the protein is expressed as a lipidated protein.

38. The method of claim 37, in which the protein of the invention is 919, 287, ORF4, 406, 576, or ORF25.

39. A method for the heterologous expression of a protein of the invention, in which (a) the protein's C-terminus region is mutated and, optionally, (b) no fusion partner is used.

40. The method of claim 39, wherein the mutation is a substitution, an insertion, or a deletion

41. The method of claim 40, wherein the protein of the invention is 730, ORF29 or ORF46.

42. A method for the heterologous expression of a protein of the invention, in which the protein's leader peptide is mutated.

43. The method of claim 42, in which the protein of the invention is 919.

44. A method for the heterologous expression of a protein, in which a poly-glycine stretch within the protein is mutated.

45. The method of claim 44, wherein the protein is a protein of the invention.

46. The method of claim 45, wherein the protein of the invention is 287, 741, 983 or Tbp2.

47. The method of claim 46, wherein $(Gly)_6$ is deleted from 287 or 983.

48. The method of claim 46, wherein $(Gly)_4$ is deleted from Tbp2 or 741

49. The method of claim 47 or claim 48, wherein the leader peptide is also deleted.

50. The method of any preceding claim, in which the heterologous expression is in an *E.coli* host.

51. A protein expressed by the method of any preceding claim.

52. A heterologous protein comprising the N-terminal amino acid sequence MKKYLFSAA.

FIGURE 1

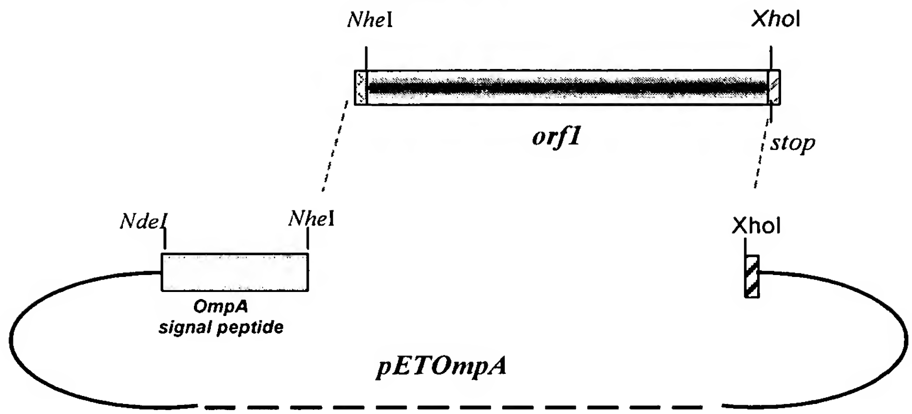


FIGURE 2

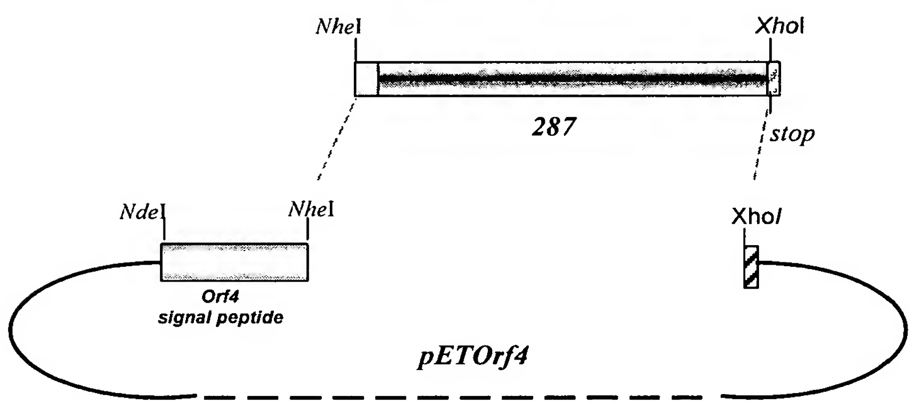
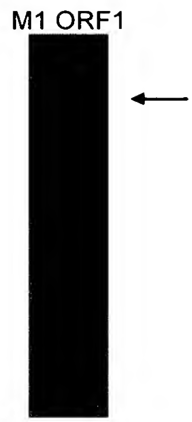
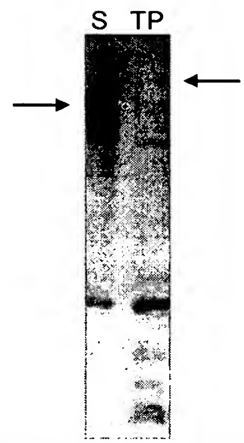


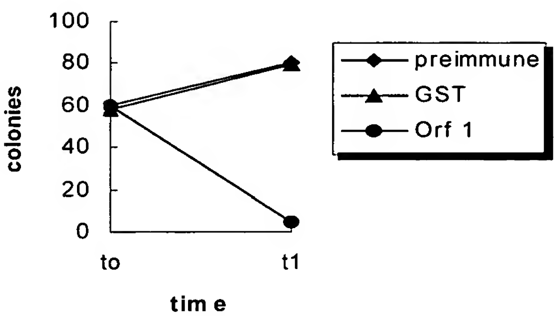
FIGURE 3



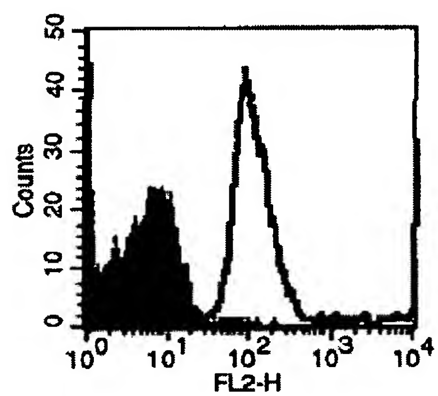
PURIFICATION



WESTERN BLOT



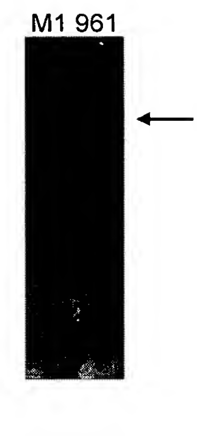
BACTERICIDAL ASSAY



FACS

ELISA: POSITIVE

FIGURE 4



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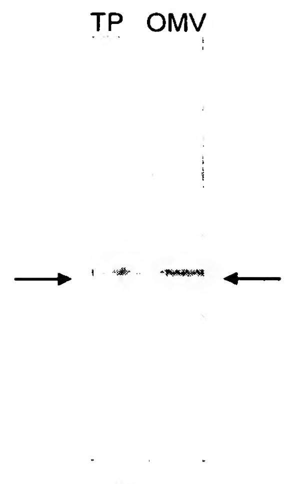

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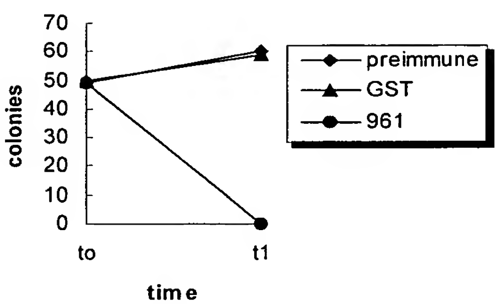
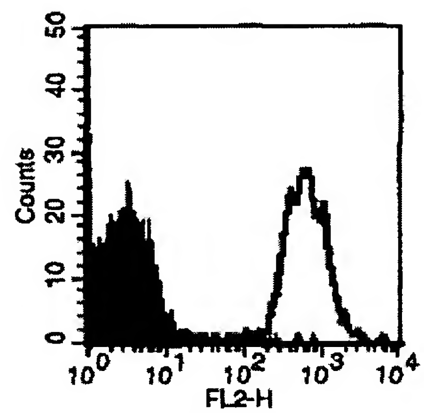


BACTERICIDAL ASSAY



FACS

ELISA: *POSITIVE*

FIGURE 5

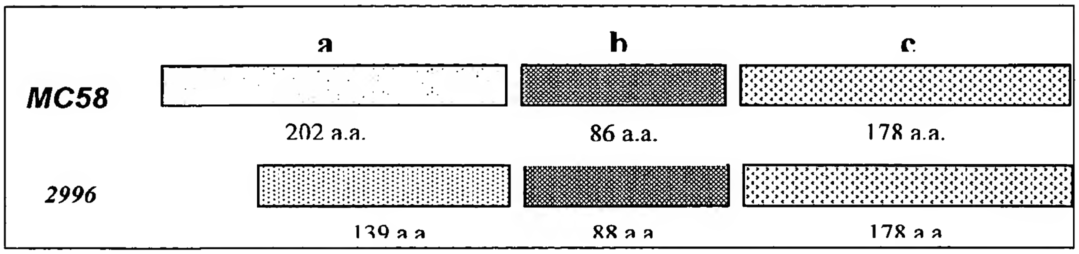


FIGURE 6

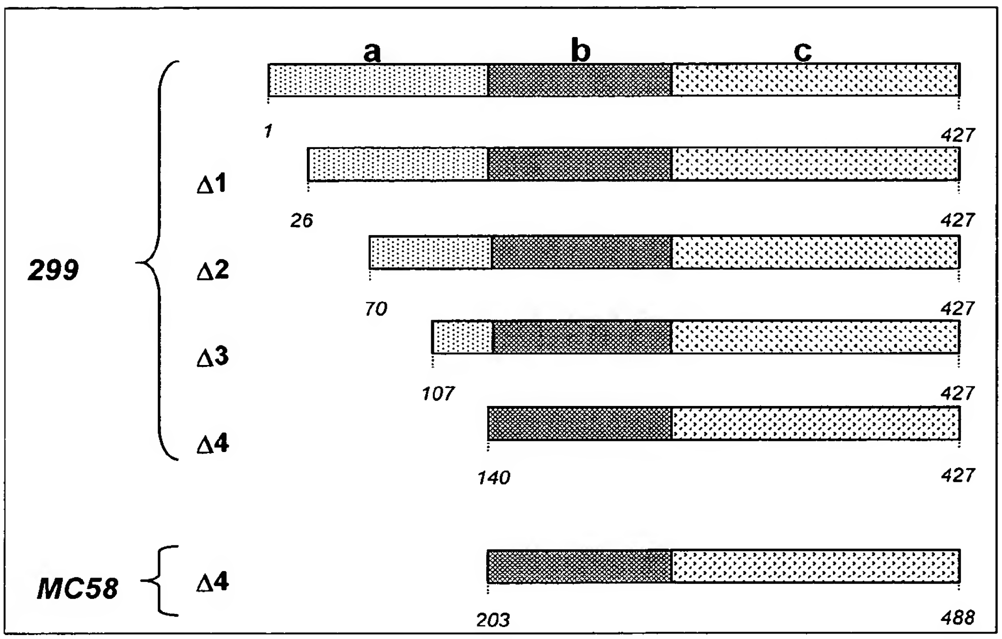


FIGURE 9

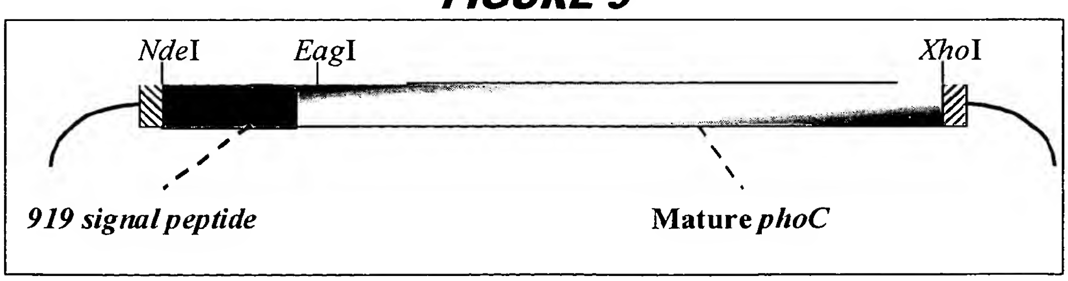


FIGURE 7

```
          <A---------------------<Δ1------------------------------
MC58   1  MFKRSVIAMACIFALSACGGGGGGSPDVKSADTLSKPAAPVVSEKETEAKEDAPQAGSQG
2996   1  MFERSVIAMACIFALSACGGGGGGSPDVKSADTLSKPAAPVVAEKETEVKEDAPQAGSQG

          --------<Δ2--------------------------------------------------
MC58  61  QGAPSAQGSQDMAAVSEENTGNGGAVTADNPKNEDEVAQNDMPQNAAGTDSSTPNHTPDP
2996  61  QGAPSTQGSQDMAAVSAENTGNGGAATTDKPKNEDEGPQNDMPQN...............

          ------------------------------------------------<Δ3--------
MC58 121  NMLAGNMENQATDAGESSQPANQPDMANAADGMQGDDPSAGGQNAGNTAAQGANQAGNNQ
2996 106  .................................................SAESANQTGNNQ

          --------------------A><B-------------------------------------
MC58 181  AAGSSDPIPASNPAPANGGSNFGRVDLANGVLIDGPSQNITLTHCKGDSCSGNNFLDEEV
2996 118  PADSSDSAPASNPAPANGGSNFGRVDLANGVLIDGPSQNITLTHCKGDSCNGDNLLDEEA

          ----------------------------------------------B>
MC58 241  QLKSEFEKLSDADKISNYKKDGKNDKFVGLVADSVQMKGINQYIIFYKPK..PTSFARFR
2996 178  PSKSEFENLNESERIEKYKKDGKSDKFTNLVATAVQANGTNKYVIIYKDKSASSSSARFR

                      <C--------------------------------------------
MC58 299  RSARSRRSLPAEMPLIPVNQADTLIVDGEAVSLTGHSGNIFAPEGNYRYLTYGAEKLPGG
2996 238  RSARSRRSLPAEMPLIPVNQADTLIVDGEAVSLTGHSGNIFAPEGNYRYLTYGAEKLPGG

          ------------------------------------------------------------
MC58 359  SYALRVQGEPAKGEMLAGAAVYNGEVLHFHTENGRPYPTRGRFAAKVDFGSKSVDGIIDS
2996 298  SYALRVQGEPAKGEMLAGTAVYNGEVLHFHTENGRPYPTRGRFAAKVDFGSKSVDGIIDS

          ------------------------------------------------------------
MC58 419  GDDLHMGTQKFKAAIDGNGFKGTWTENGSGDVSGKFYGPAGEEVAGKYSYRPTDAEKGGF
2996 358  GDDLHMGTQKFKAAIDGNGFKGTWTENGGGDVSGRFYGPAGEEVAGKYSYRPTDAEKGGF

          --------C>
MC58 479  GVFAGKKEQD*
2996 418  GVFAGKKEQD*
```

FIGURE 8

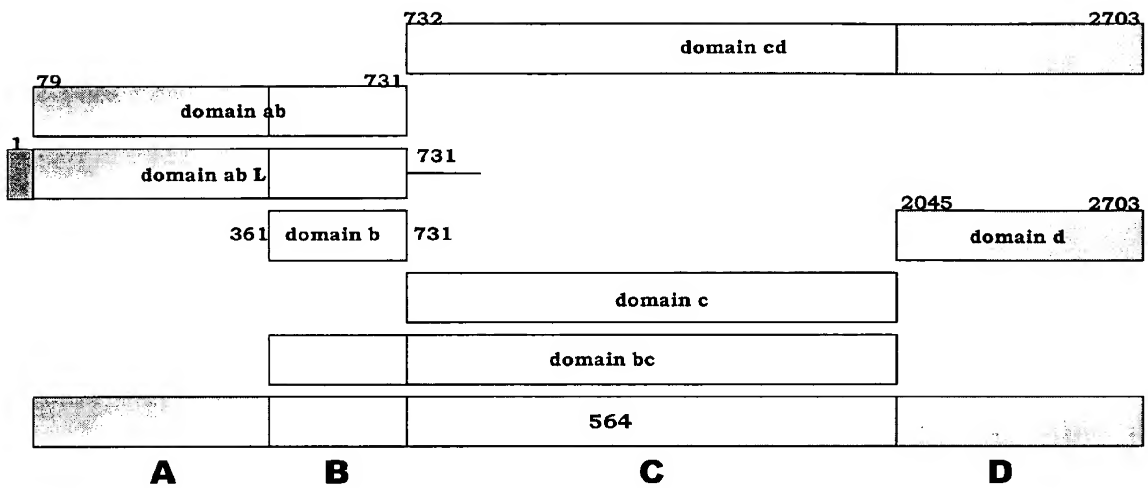


FIGURE 10

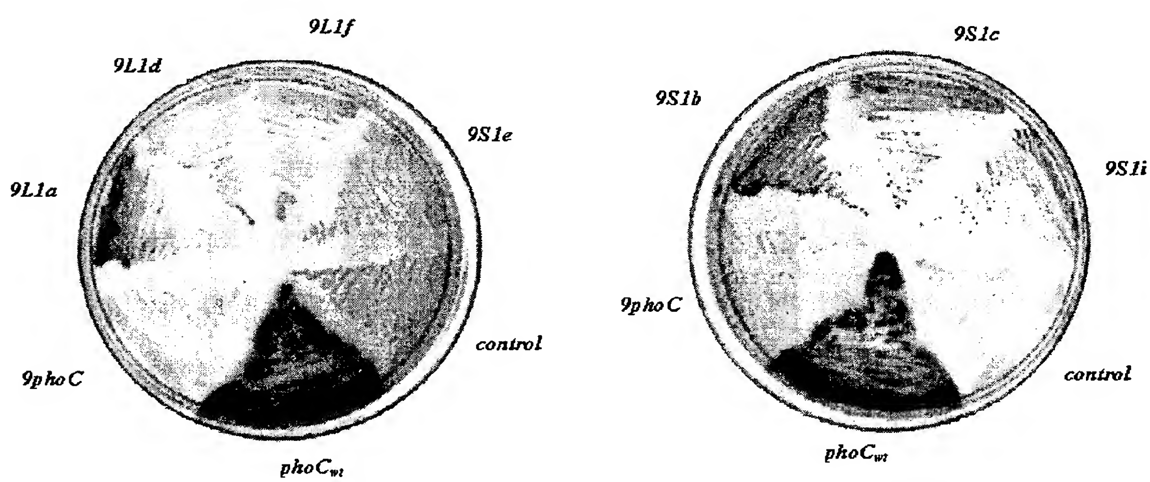


FIGURE 11A

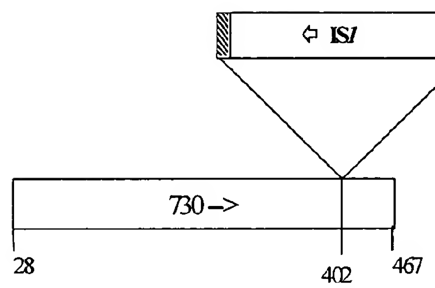


FIGURE 11B

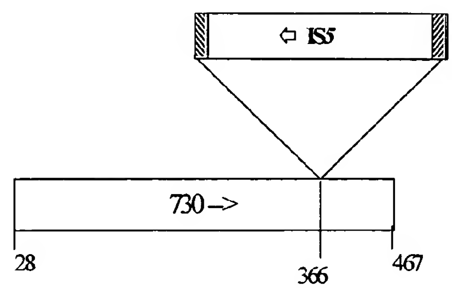


FIGURE 12

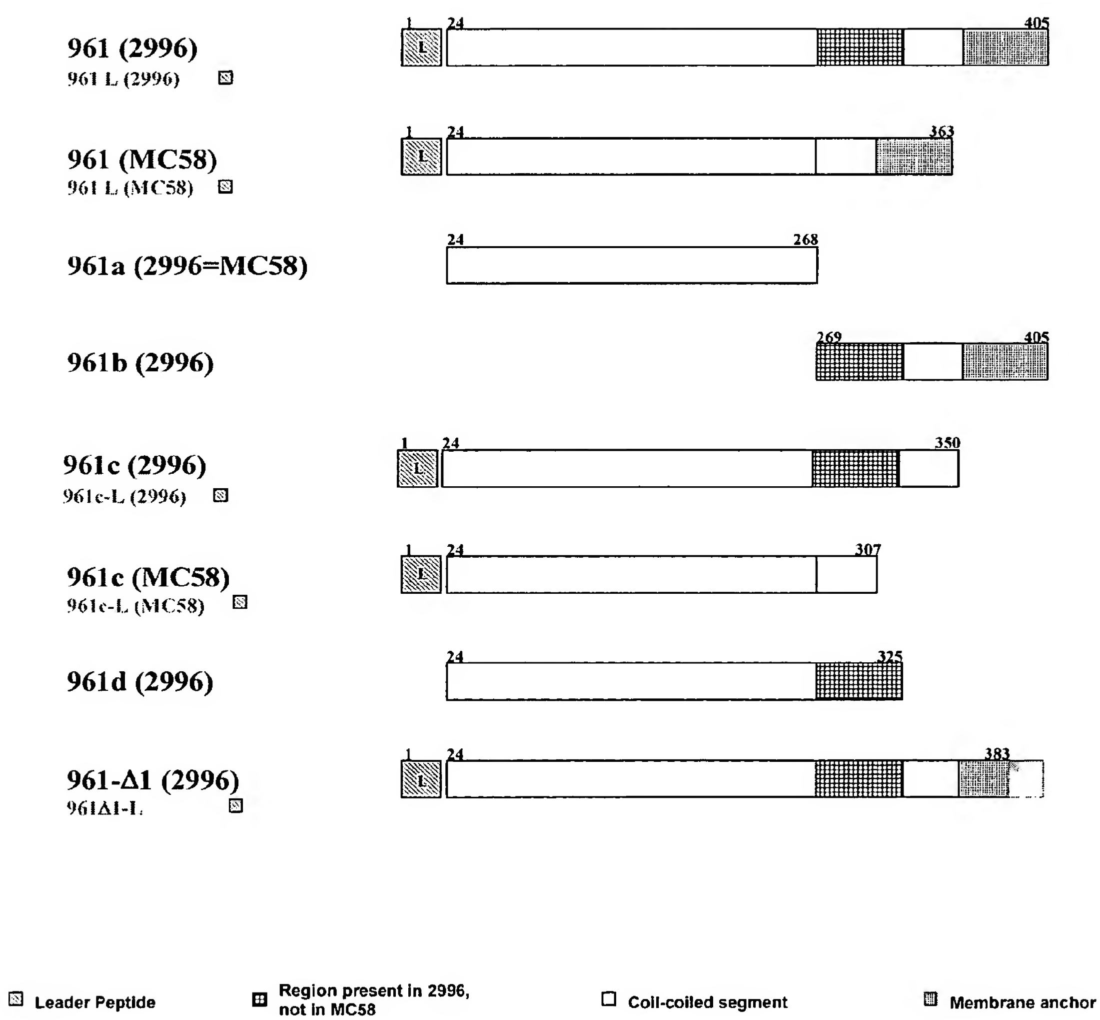


FIGURE 13

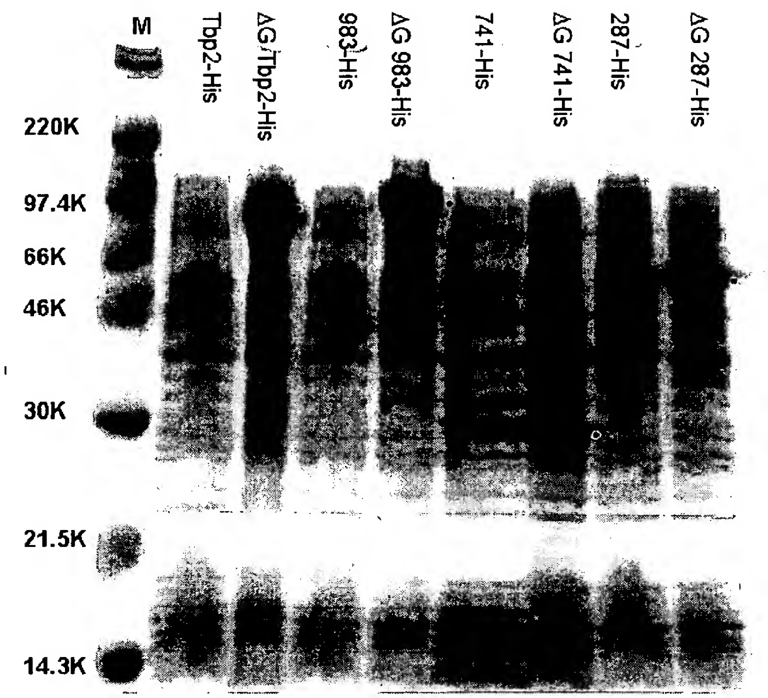


FIGURE 14

FIGURE 14A — ΔG287—919

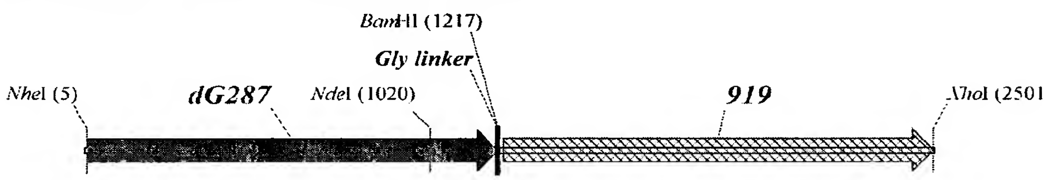


FIGURE 14B — ΔG287—953

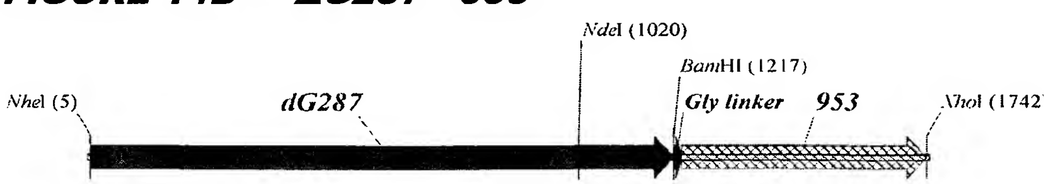


FIGURE 14C — ΔG287—961

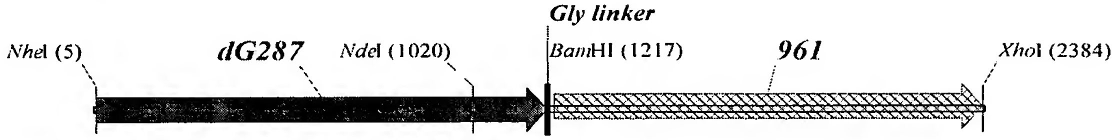


FIGURE 14D — ΔG287NZ—919

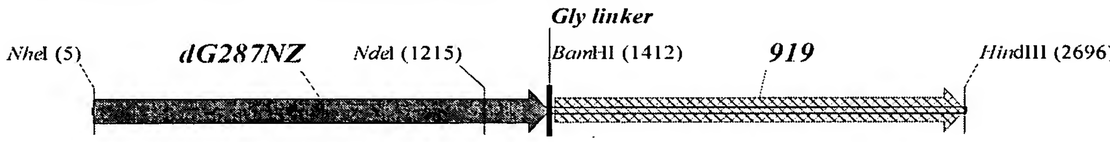


FIGURE 14E — ΔG287NZ—953

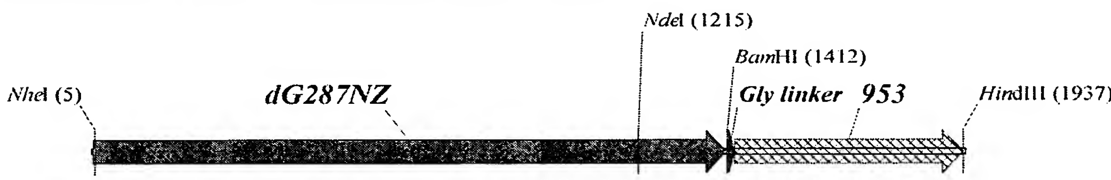


FIGURE 14F — ΔG287NZ—961

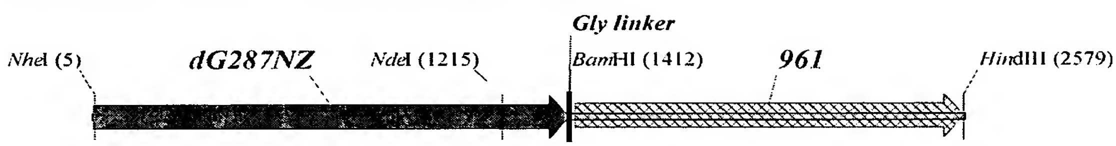


FIGURE 14G — ΔG983-ORF46.1

FIGURE 14H — ΔG983-741

FIGURE 14I — ΔG983-961

FIGURE 14J — ΔG983-961c

FIGURE 14K — ΔG741-961

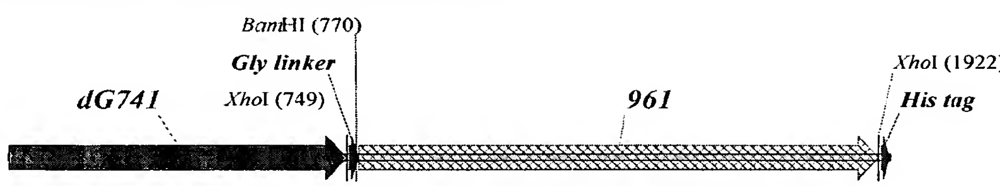


FIGURE 14L — ΔG741-961c

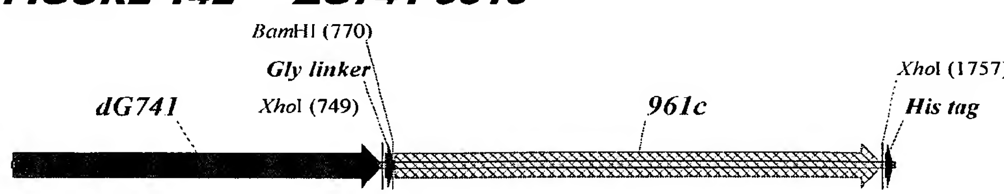


FIGURE 14M — ΔG741-983

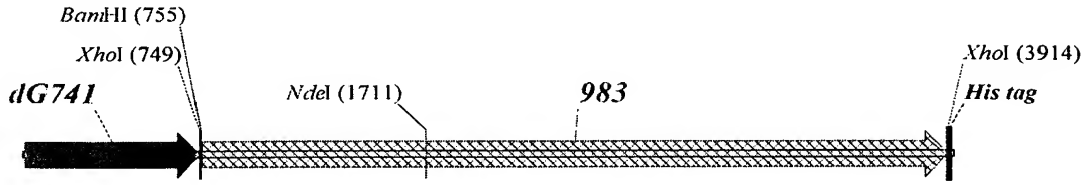


FIGURE 14N — ΔG741-ORF46.1

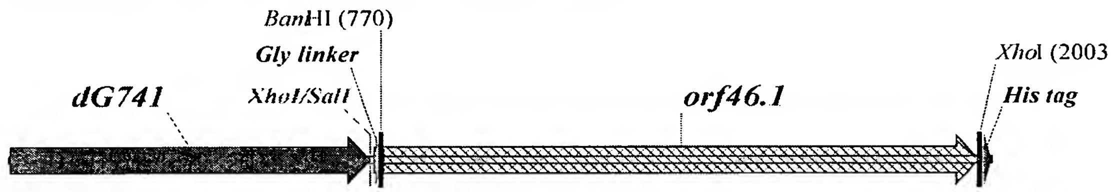


FIGURE 14O — ORF46.1-741

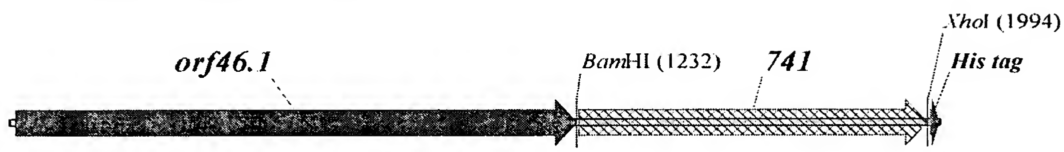


FIGURE 14P — ORF46.1-961

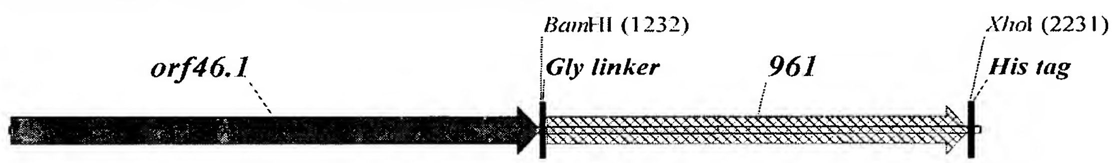


FIGURE 14Q — ORF46.1—961c

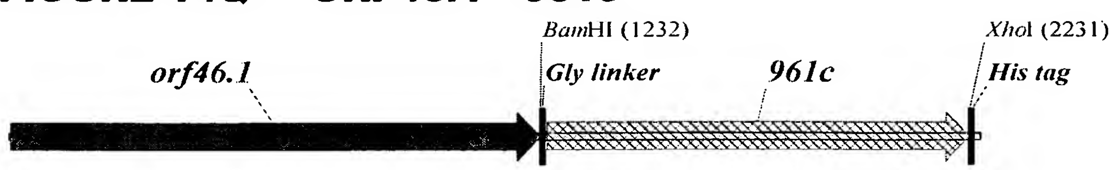


FIGURE 14R — 961-ORF46.1

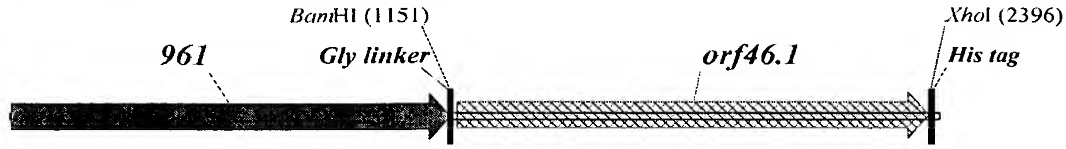


FIGURE 14S — 961-741

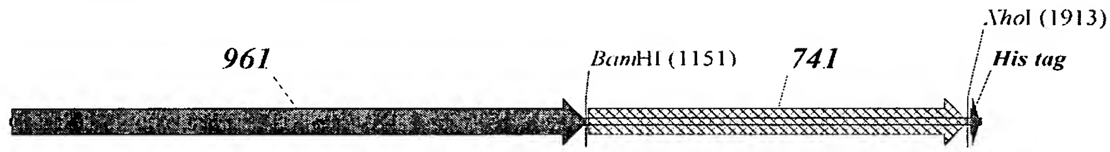


FIGURE 14T — 961-983

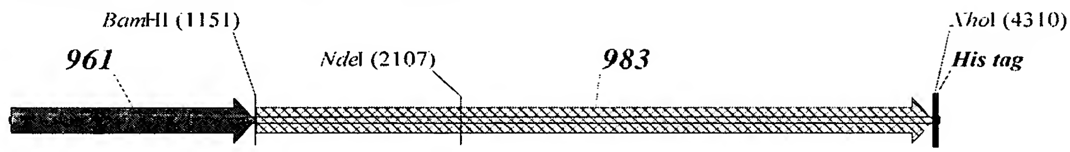


FIGURE 14U — 961c-ORF46.1

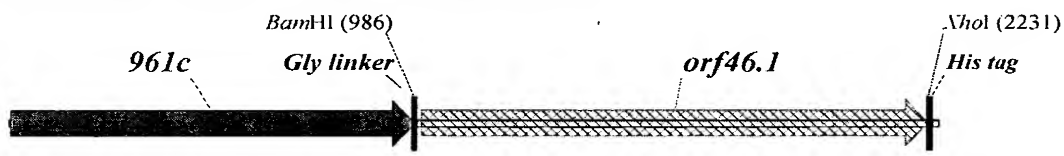


FIGURE 14V — 961c-741

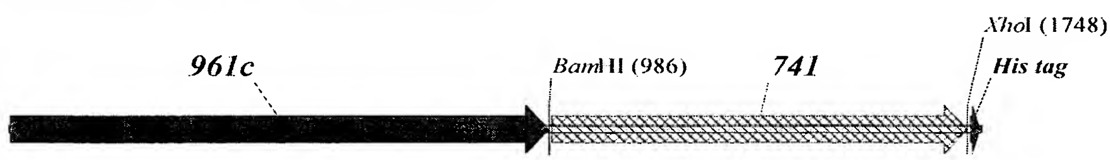


FIGURE 14W — 961c-983

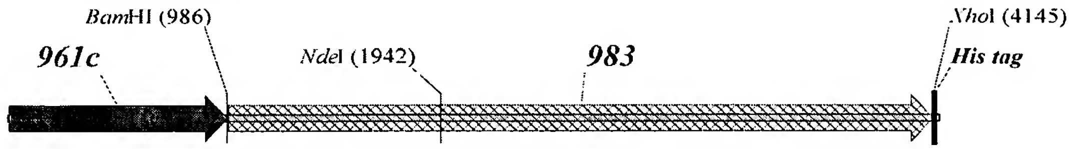


FIGURE 14X — 961cL-ORF46.1

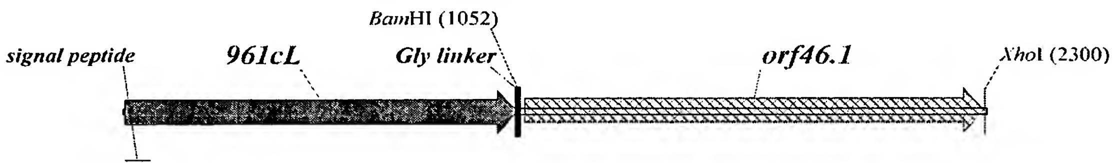


FIGURE 14Y — 961cL-741

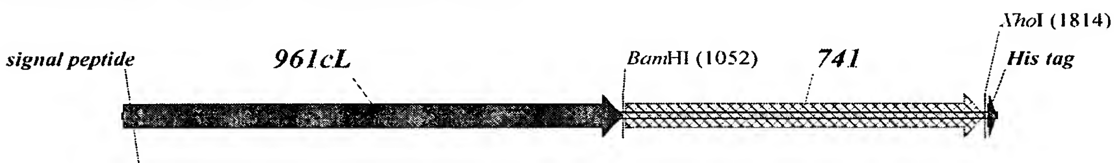
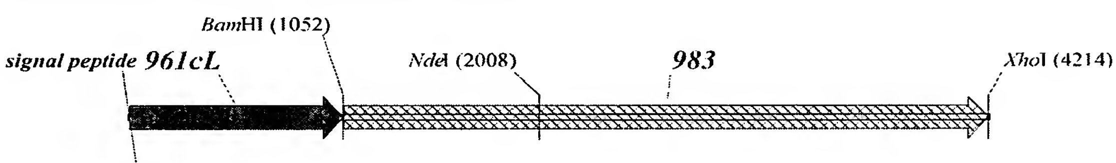


FIGURE 14Z — 961cL-983



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